

STIC Search Report Biotech-Chem Library

STIC Database Tracking Number 1999

TO: Kevin Weddington Location: rem/3a65/3c70

Art Unit: 1614

Wednesday, August 17, 2005

Case Serial Number: 10/631029

From: Mary Hale

Location: Biotech/Chem Library

Rem 1D86 Phone: 2-2507

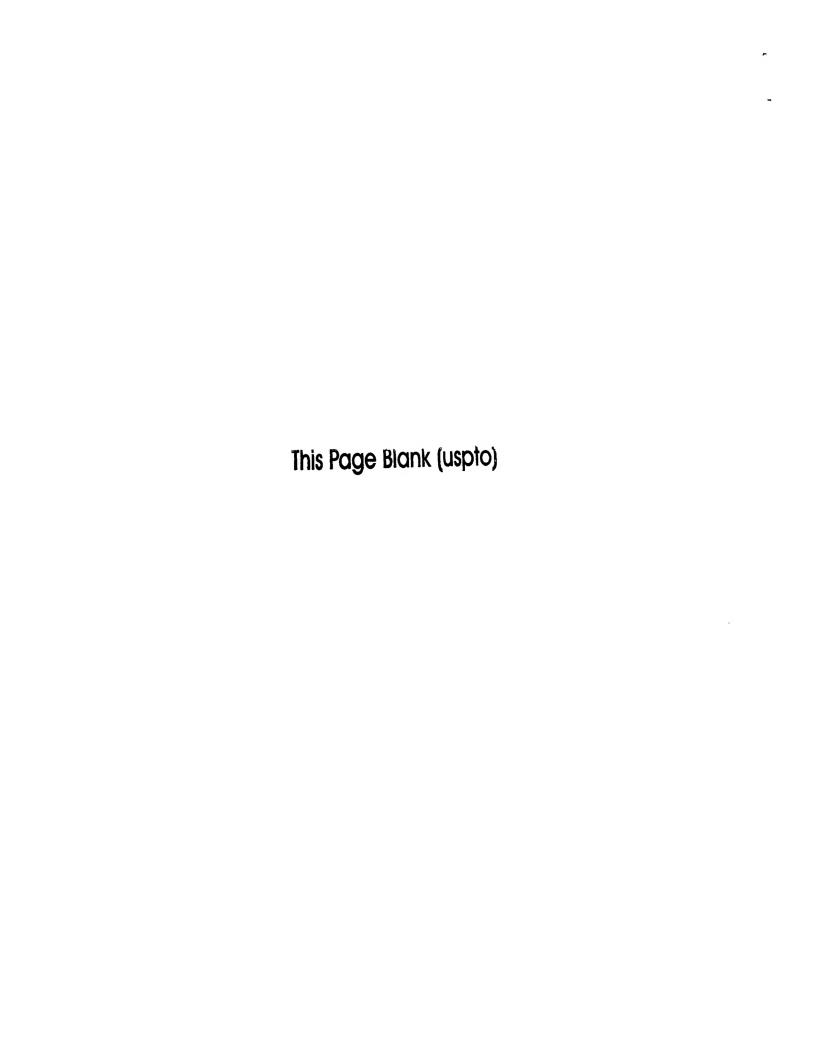
Mary.Hale@uspto.gov

Search Notes

Feel free to contact me if you have any questions.

Note -- results are printed on both sides of printout





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Scientific and Technical Information Center

SEARCH REQUEST FORM

Requester's Full Name: K. W. Art Unit: \\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\	lumber: 2-0587	Seria Results Forn	#: <u>\&0\&2</u> il Number: nat Preferred	10 6 31, 0 (circle):(PAP	ER DISK	
To ensure an efficient and quality search, ple	ease attach a copy of the co	ver sheet, claim	s, and abstract o	r fill out the fol	lowing:	81
Title of Invention:						1
Inventors (please provide full names):	Rajinder Sing	h; Ank	such Argo	ade; Don	ald O. F	Ryan'
Holger Kein; Somase						
Earliest Priority Date:		` /				
Search Topic: Please provide a detailed statement of the sear elected species or structures, keywords, synony Define any terms that may have a special mean	ms, acronyms, and registry i	numbers, and co	ombine with the c	concept or utility		
For Sequence Searches Only Please include appropriate serial number.	e all pertinent information (p	parent, child, di	visional, or issue	d patent number	s) along with the	
	une disease	With	a 2,4-p	yrimidir	rediamine	compuner
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Date Searcher Picked Up:	Bibliographic		In-house seque			
			Commercial	Oligomer	Score/Length	
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=> fil reg COST IN U.S. DOLLARS

SINCE FILE TOTAL ENTRY SESSION 0.21 0.21

FULL ESTIMATED COST

FILE 'REGISTRY' ENTERED AT 10:15:38 ON 17 AUG 2005 USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT. PLEASE SEE "HELP USAGETERMS" FOR DETAILS. COPYRIGHT (C) 2005 American Chemical Society (ACS)

Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 16 AUG 2005 HIGHEST RN 860495-66-5 DICTIONARY FILE UPDATES: 16 AUG 2005 HIGHEST RN 860495-66-5

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH JANUARY 18, 2005

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Structure search iteration limits have been increased. See HELP SLIMITS for details.

Experimental and calculated property data are now available. For more information enter HELP PROP at an arrow prompt in the file or refer to the file summary sheet on the web at: http://www.cas.org/ONLINE/DBSS/registryss.html

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L1 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2005 ACS on STN
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RN 156-81-0 REGISTRY

ED Entered STN: 16 Nov 1984

CN 2,4-Pyrimidinediamine (9CI) (CA INDEX NAME)

```
Page 2
OTHER CA INDEX NAMES:
     Pyrimidine, 2,4-diamino- (6CI, 7CI, 8CI)
OTHER NAMES:
     2,4-Diaminopyrimidine
CN
     NSC 30856
CN
FS
     3D CONCORD
     42910-88-3, 42910-89-4, 42910-90-7, 42910-92-9
DR
MF
     C4 H6 N4
CI
     COM
                   AGRICOLA, ANABSTR, BEILSTEIN*, BIOBUSINESS, BIOSIS, CA,
LC
     STN Files:
       CANCERLIT, CAOLD, CAPLUS, CASREACT, CHEMCATS, CHEMLIST, CSCHEM, EMBASE,
       MEDLINE, SPECINFO, TOXCENTER, USPAT2, USPATFULL
          (*File contains numerically searchable property data)
                       EINECS**
     Other Sources:
         (**Enter CHEMLIST File for up-to-date regulatory information)
             NH<sub>2</sub>
H<sub>2</sub>N
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PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

254 REFERENCES IN FILE CA (1907 TO DATE) 44 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA 254 REFERENCES IN FILE CAPLUS (1907 TO DATE) 7 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

1: 143:138607 REFERENCE

REFERENCE 2: 143:72294

REFERENCE 3: 142:254587

REFERENCE 142:212327 4:

REFERENCE 5: 142:74474

REFERENCE 6: 142:38288

REFERENCE 7: 141:260782

REFERENCE 8: 141:93976

REFERENCE 9: 141:76686

REFERENCE 10: 141:76353

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E1 1 R 91650/CN E2 R 920K/CN E3 0 --> R 921302/CN R 922/CN E4 1 R 922-1/CN E5

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            1
E2
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E4
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L15

L16

L17

L18

R9F5/CN => fil medl, biosis, embase, caplus TOTAL SINCE FILE COST IN U.S. DOLLARS ENTRY SESSION 7.96 8.17 FULL ESTIMATED COST FILE 'MEDLINE' ENTERED AT 10:17:20 ON 17 AUG 2005 FILE 'BIOSIS' ENTERED AT 10:17:20 ON 17 AUG 2005 Copyright (c) 2005 The Thomson Corporation FILE 'EMBASE' ENTERED AT 10:17:20 ON 17 AUG 2005 COPYRIGHT (C) 2005 Elsevier Inc. All rights reserved. FILE 'CAPLUS' ENTERED AT 10:17:20 ON 17 AUG 2005 USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT. PLEASE SEE "HELP USAGETERMS" FOR DETAILS. COPYRIGHT (C) 2005 AMERICAN CHEMICAL SOCIETY (ACS) => s (autoimmune disease or autoimmune encephalomyelit? or rheumatoid arthrit? or systemic lupus erythematos? or multiple sclerosis) 136215 FILE MEDLINE L2119817 FILE BIOSIS L3 136957 FILE EMBASE T.4 60193 FILE CAPLUS L5 TOTAL FOR ALL FILES 453182 (AUTOIMMUNE DISEASE OR AUTOIMMUNE ENCEPHALOMYELIT? OR RHEUMATOID 1.6 ARTHRIT? OR SYSTEMIC LUPUS ERYTHEMATOS? OR MULTIPLE SCLEROSIS) => s c20.111?O FILE MEDLINE L7 0 FILE BIOSIS L80 FILE EMBASE TERM '111?' EXCEEDED TRUNCATION LIMITS - SEARCH ENDED You have entered a truncated stem which occurs in too many terms. Make the stem longer and try again. For example, if your original term was 'degr?' to search for variations and the abbreviation for 'degradation', you could replace it with the expression '(degrdn OR degrad?)'. If your search term was numeric, e.g., 'C>5', reduce the size of the range. => s c20.111?/ct 250623 FILE MEDLINE L1050150 FILE BIOSIS L11O FILE EMBASE L12 0 FILE CAPLUS L13 TOTAL FOR ALL FILES 300773 C20.111?/CT L14 => s l1 or "2,4-pyrimidinediamine" or "2,4-diaminopyridine" or nsc 30856 or r(w) (921302 or 926891 or 940323 or 940347 or 921303) or r921302 or r926891 or r940323 or r940347 or r921303 39 FILE MEDLINE

62 FILE BIOSIS

35 FILE EMBASE

351 FILE CAPLUS

L22 0 FILE MEDLINE
L23 0 FILE BIOSIS
L24 1 FILE EMBASE
L25 12 FILE CAPLUS

TOTAL FOR ALL FILES L26 13 L19 AND (L6 OR L14)

=> d 1-13 ibib abs hitstr

L27 ANSWER 1 OF 13 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2005:158647 CAPLUS

DOCUMENT NUMBER: 142:261547

TITLE: Preparation of 2,4-

pyrimidinediamines useful in the treatment of

neoplastic diseases, inflammatory and immune system

disorders

INVENTOR(S): Garcia-echeverria, Carlos; Kanazawa, Takanori;

Kawahara, Eiji; Masuya, Keiichi; Matsuura, Naoko; Miyake, Takahiro; Ohmori, Osamu; Umemura, Ichiro; Steensma, Ruo; Chopiuk, Greg; Jiang, Jiqing; Wan, Yongqin; Ding, Qiang; Zhang, Qiong; Gray, Nathanael

Schiander; Karanewsky, Donald

PATENT ASSIGNEE(S): Novartis A.-G., Switz.; Novartis Pharma G.m.b.H.; IRM

LLC

SOURCE: PCT Int. Appl., 285 pp.

CODEN: PIXXD2

DOCUMENT TYPE: LANGUAGE: Patent English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND DATE	APPLICATION NO.	DATE
WO 2005016894	A1 20050224	WO 2004-EP9099	20040813
W: AE, AG, AL,	AM, AT, AU, AZ,	BA, BB, BG, BR, BW, BY,	BZ, CA, CH,
CN, CO, CR,	CU, CZ, DE, DK,	DM, DZ, EC, EE, EG, ES,	FI, GB, GD,
GE, GH, GM,	HR, HU, ID, IL,	IN, IS, JP, KE, KG, KP,	KR, KZ, LC,
LK, LR, LS,	LT, LU, LV, MA,	MD, MG, MK, MN, MW, MX,	MZ, NA, NI,
NO, NZ, OM,	PG, PH, PL, PT,	RO, RU, SC, SD, SE, SG,	SK, SL, SY,
TJ, TM, TN,	TR, TT, TZ, UA,	UG, US, UZ, VC, VN, YU,	ZA, ZM, ZW
RW: BW, GH, GM,	KE, LS, MW, MZ,	NA, SD, SL, SZ, TZ, UG,	ZM, ZW, AM,
AZ, BY, KG,	KZ, MD, RU, TJ,	TM, AT, BE, BG, CH, CY,	CZ, DE, DK,
EE, ES, FI,	FR, GB, GR, HU,	IE, IT, LU, MC, NL, PL,	PT, RO, SE,

SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE,

SN, TD, TG

A 20030815 GB 2003-19227 PRIORITY APPLN. INFO.: GB 2003-22370 A 20030924

OTHER SOURCE(S):

MARPAT 142:261547

GΙ

$$\begin{array}{c|c} O_2N & N \\ \hline & N \\ NH & NH \\ \hline & OMe \\ \hline & MeO \\ \hline & II \\ \end{array}$$

The title compds. I [R = aryl, heteroaryl, cycloalkyl and AB heterocycloalkyl; R0-R3 = H, alkyl, cycloalkyl, etc.; R4 = H, alkyl; R5, R6 = H, alkyl, alkoxyalkyl, etc.], useful for the manufacture of a medicament for the treatment or prevention of a disease which responds to inhibition of FAK and/or ALK and/or ZAP-70 and/or IGF-IR, were prepared and formulated. E.g., a 2-step synthesis of II, starting from 2,4-dichloro-5nitropyrimidine and 2-amino-N-methylbenzenesulfonamide, was given. compds. I have IC50 values in the range of 10 nM to 2 μM in cell-free ZAP-70 kinase assay.

THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS REFERENCE COUNT: 19 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L27 ANSWER 2 OF 13 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER:

2005:158646 CAPLUS

DOCUMENT NUMBER:

142:254587

TITLE:

Methods for treating or preventing autoimmune

diseases with 2,4-

pyrimidinediamine compounds

Rajinder, Singh; Ankush, Argade; Li, Hui; Bhamidipati, INVENTOR(S):

Somasekhar; Carroll, David; Sylvain, Catherine;

Clough, Jeffrey; Keim, Holger Rigel Pharmaceuticals, Inc., USA

PATENT ASSIGNEE(S):

SOURCE:

PCT Int. Appl., 276 pp.

CODEN: PIXXD2

DOCUMENT TYPE:

Patent English LANGUAGE:

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

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KIND
                               DATE
                                          APPLICATION NO.
    PATENT NO.
                        ----
                                           -----
    WO 2005016893
                        A2
                               20050224
                                           WO 2004-US24716
                               20050609
    WO 2005016893
                        A3
           AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
            CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
            GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,
            LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI,
            NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY,
            TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
        RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM,
            AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK,
            EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE,
            SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE,
            SN, TD, TG
PRIORITY APPLN. INFO.:
                                           US 2003-491641P
                                                               P 20030730
                                                           P 20031219
                                           US 2003-531598P
                                                              P 20040518
                                           US 2004-572246P
OTHER SOURCE(S):
                        MARPAT 142:254587
    The invention provides methods for treating or preventing
     autoimmune diseases with 2,4-
    pyrimidinediamine compds., as well as methods of treating,
    preventing or ameliorating symptoms associated with such diseases.
     examples of autoimmune diseases that can be treated or
    prevented with the compds. include rheumatoid arthritis
     and/or its associated symptoms, systemic lupus
     erythematosis and/or its associated symptoms and multiple
     sclerosis and/or its associated symptoms.
    156-81-0D, 2,4-Pyrimidinediamine,
IT
    derivs.
    RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
     (Biological study); USES (Uses)
        (pyrimidinediamine compds. for treatment or prevention of
       autoimmune diseases)
    156-81-0 CAPLUS
RN
    2,4-Pyrimidinediamine (9CI) (CA INDEX NAME)
CN
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DOCUMENT TYPE:

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L27 ANSWER 3 OF 13 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER:
                         2005:120923 CAPLUS
DOCUMENT NUMBER:
                         142:219300
TITLE:
                         2,4-Pyrimidinediamines
                         for use in the treatment or prevention of
                         autoimmune diseases
                         Rajinder, Singh; Ankush, Argade; Li, Hui; Bhamidipati,
INVENTOR(S):
                         Somasekhar; Carroll, David; Sylvain, Catherine;
                         Clough, Jeffrey; Keim, Holger
                         Rigel Pharmaceuticals, Inc., USA
PATENT ASSIGNEE(S):
                         PCT Int. Appl., 169 pp.
SOURCE:
                         CODEN: PIXXD2
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Prepared by: Mary Hale @2-2507 Rem Bldg 1D86

Patent

Page 8

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 3

PATENT INFORMATION:

PA'	PATENT NO.						DATE		1	APPL	ICAT:	ION 1	. 01		D	ATE	
						-									-		
WO	2005	0122	94		A1		2005	0210	1	WO 2	004-1	JS24	920		2	0040	730
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		CN,	CO,	CR,	CU,	CZ,	DE,	DK,	DM,	DZ,	EC,	ΕĒ,	EG,	ES,	FI,	GB,	GD,
		GE,	GH,	GM,	HR,	HU,	ID,	IL,	IN,	IS,	JP,	KΕ,	KG,	ΚP,	KR,	ΚZ,	LC,
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	TJ, TM, TN,		TR,	TT,	ΤZ,	UΑ,	ŪĠ,	US,	UΖ,	VC,	VN,	YU,	ZA,	ZM,	zw		
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PRIORIT	PRIORITY APPLN. INFO.:									US 2	003-	4916	41P	1	P 2	0030	730
									•	US 2	003-	5315	98P		P 2	0031	219
									•	US 2	004-	5722	46P	:	P 2	0040	518

OTHER SOURCE(S):

MARPAT 142:219300

GΙ

The present invention provides methods of treating or preventing AB autoimmune diseases with 2,4pyrimidinediamine compds. I [L1, L2 = a direct bond or a linker; R2 = II; R4 = III; X = N, CH; Y, Z = O, S, SO, SO2, etc.; R5 = R6, alkyl,alkenyl, etc.; R6 = H, an electroneg. group, alkoxy, haloalkoxy, etc.; R31 = Me, alkyl; R35 = H, alkyl, cycloalkyl, etc.; or two R35 bonded together to the same carbon atom are taken together to form an oxo, (un) substituted NH], as well as methods of treating, preventing or ameliorating symptoms associated with such diseases. Specific examples of autoimmune diseases that can be treated or prevented with the compds. I include rheumatoid arthritis and/or its associated symptoms, systemic lupus erythematosus and/or its associated symptoms and multiple sclerosis and/or its associated symptoms. The general procedures for synthesis of compds. I are described. The characterization data for over 500 prepared

compds. I were given in table. The compds. I were tested in various tests (e.g., inhibition of IgE-induced degranulation, inhibition of Syk kinase, etc.). For example, N4-(2,2-dimethyl-3-oxo-4H-5-pyrido[1,4]oxazin-6-yl)-5fluoro-N2-(3,4,5-trimethoxyphenyl)-2,4-

pyrimidinediamine showed 99.8% inhibition of edema formation when administered at 5 mg/kg in mice.

REFERENCE COUNT:

THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L27 ANSWER 4 OF 13 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER:

2004:220155 CAPLUS

DOCUMENT NUMBER:

140:270866

TITLE:

Preparation of (pyridinyl) (pyrimidinyl) imidazo[1,2alpyridines as TGFB receptor type I antagonists for treatment of fibrotic disorders and tumors

INVENTOR(S):

Lee, Wen-cherng; Carter, Mary Beth; Sun, Lihong; Chuaqui, Claudio; Singh, Juswinder; Boriack-Sjodin,

ADDITCATION NO

בו איניים

Paula; Choi, Michael S.

PATENT ASSIGNEE(S):

Biogen, Inc., USA

חאיד

SOURCE:

PCT Int. Appl., 142 pp. CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

English

KIND

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION: DATENT NO

	PATENT NO.				KINI		DATE						NO.			ATE		
		2004						2004									0030	
	WO	2004	0219	89		A 3		2004	0923									
		W:	ΑE,	AG,	AL,	AM,	ΑT,	AU,	ΑZ,	BA,	BB,	BG,	BR,	BY,	ΒŻ,	CA,	CH,	CN,
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			PG,	PH,	PL,	PT,	RO,	RU,	SC,	SD,	SE,	SG,	SK,	SL,	SY,	ТJ,	TM,	TN,
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		RW:	GH,	GM,	KE,	LS,	MW,	MZ,	SD,	SL,	SZ,	TZ,	UG,	ZM,	ZW,	AM,	ΑZ,	BY,
			KG,	KZ,	MD,	RU,	ТJ,	TM,	ΑT,	BE,	BG,	CH,	CY,	CZ,	DE,	DK,	EE,	ES,
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	EP	1546	112			A2		2005	0629	:	EP 2	003-	7520	04		2	0030	905
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OTHE	R SC	DURCE	(S):			MARI	TAG	140:	27086	56								

OTHER SOURCE(S):

GΙ

Title compds. I [wherein X1, X2, X3, X4 = independently CRx or N, only two AB of them can be N simultaneously; Y1, Y2 = independently CRa or N, at least one of them must be N; R1 = independently alkyl, alkenyl, alkynyl, alkoxy, acyl, urea, cycloalkylsulfanyl, etc.; R2 = independently alkyl, alkenyl, alkynyl, acyl, halo, -N(alkyl)(cycloalkyl), heteroaroyl, etc.; m = 0-4; n = 0-3; Rx, Ra = independently hydrogen, alkyl, alkenyl, hydroxy, guanidino, amidino, cycloalkylcarbonylamino, etc.; and pharmaceutically acceptable salts or N-oxides thereof] were prepared as antagonists against transforming growth factor β (TGF β) family type I receptors, Alk5 and Alk4. For example, methylation of 2-mercapto-4-methylpyrimidine with MeI, followed by reaction with 6-methylpyridine-2-carboxylic acid Et ester and cyclocondensation with 2-aminopyridine, gave II. I exhibited $TGF\beta$ -induced PAI-Luciferase reporter activity with IC50 values of less than $10\mu M$ and cytotoxicity with LD25 values greater than $10\mu M$. Thus, I and their pharmaceutical compns. are useful as antagonists for preventing and/or treating numerous diseases, including fibrotic disorders and tumors.

IT 156-81-0, 2,4-Diaminopyrimidine

RL: RCT (Reactant); RACT (Reactant or reagent) (preparation of (pyridinyl) (pyrimidinyl) imidazo[1,2-a]pyridines as TGFβ receptor type I antagonists for treatment of fibrotic disorders and tumors)

RN 156-81-0 CAPLUS

CN 2,4-Pyrimidinediamine (9CI) (CA INDEX NAME)

L27 ANSWER 5 OF 13 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2004:142963 CAPLUS

DOCUMENT NUMBER: 140:199334

TITLE: Preparation of 2,4-pyrimidinediamines as IgE and/or

IgG receptor modulators for treatment of autoimmune

diseases

INVENTOR(S): Singh, Rajinder; Argade, Ankush; Payan, Donald G.;

Clough, Jeffrey; Keim, Holger; Sylvain, Catherine; Li,

Hui; Bhamidipati, Somasekhar

PATENT ASSIGNEE(S): Rigel Pharmaceuticals, USA

SOURCE: PCT Int. Appl., 811 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2 PATENT INFORMATION:

PA.	rent 1	NO.							1	APPI	LICAT	ION	NO.		D	ATE	
WO	2004	0143	82		A1		2004		1	 WO 2	2003-1	JS24	087		2	0030	 729
	W:	•	•	•	•	•	•	•	•	•	, BG,	•	•	•	•	•	•
		•	•	•	•	•	•	•	•		, EE, , KG,	•	•	-	-	•	•
		•	•	•	•	•	•	•	•		, NG, , MW,	•	•	•	•	•	•
			•	•	•	•	•	•	•		, SG,	•	•	•	•	•	•
											YU,				,		
	RW:	•	•	•	•	•	•	•	•		TZ,	•			AM,	ΑZ,	BY,
		KG,	KZ,	MD,	RU,	TJ,	TM,	AT,	BE,	BG,	CH,	CY,	CZ,	DE,	DK,	EE,	ES,
		FI,	FR,	GB,	GR,	HU,	ΙE,	IT,	LU,	MC,	, NL,	PT,	RO,	SE,	SI,	SK,	TR,
		BF,	ВJ,	CF,	CG,	CI,	CM,	GΑ,	GN,	GQ,	, GW,	ML,	MR,	ΝE,	SN,	TD,	TG
	2492				AA			-			2003-2						
EP	1534				A1						5003						
	R:	•	•	•		•			•		, IT,	•	•	•			PT,
	0000	•	•	•	•	•	•		•		TR,	•	•	•			700
	2003										2003-1						
	2005										2004 - 8					0040	
PRIORITY					A		2005	0329	1	11C 1	2005-2 2002-2	2006	72 D			0020	
PRIORII	I MPF.	□1N • .	INFO	• •					ì	נוס מ	2002 2003 - 4	1439	/ 3 F 4 9 D		D 2	0030	-
											2003-4					0030	
											2003-6					0030	
											2002-3	3532	67P		P 2	0020	201
											2002-3	3533	33P		P 2	0020	201
									1	US 2	2002-4	4342	77P		P 2	0021	217
									1	US 2	2003-3	3555	43	1	A1 2	0030	131
									1	WO 2	2003-1	JS24	087	1	₩ 2	0030	729

OTHER SOURCE(S):

MARPAT 140:199334

GI

AB The present invention provides methods of treating or preventing autoimmune diseases with 2,4-pyrimidinediamine compds., as well as methods of treating, preventing or ameliorating symptoms associated with such diseases. Title compds. I [wherein L1 and L2 = independently a bond or a

linker; R2 = (un)substituted alkyl, (hetero)cycloalkyl, or (hetero)aryl; R4 = H or R2; R5 = R6 or (un) substituted alkyl, alkenyl, or alkynyl; R6 = independently H, an electroneg. group, protected alc. or thiol, haloalkyl(oxy), halo, CN, NC, OCN, SCN, NO, NO2, N3, or (un) substituted amino, sulfamoyl(oxy), acyl, carboxy, carbamoyl, (hetero)aryl(alkyl), etc.; with provisos and exclusions; and salts, hydrates, solvates, N-oxides, and prodrugs thereof] were prepared as inhibitors of the IgE and/or IgG receptor signaling cascades that lead to the release of chemical mediators. For example, coupling of 2,4-dichloropyrimidine with 4-ethoxyaniline in EtOH provided N2, N4-bis(4-ethoxyphenyl)-2,4pyrimidinediamine (II). The latter inhibited degranulation of bone marrow derived mast cells challenged with anti-IgE and ionomycin with IC50 values of 4.5 μM and 4.4 μM , resp. Thus, I and their pharmaceutical compns. are useful in the treatment and prevention of diseases characterized by, caused by, or associated with the release of chemical mediators via degranulation of mast, basophil, neutrophil, or eosinophil cells and other processes effected by activation of the IgE and/or IgG receptor signaling cascades. Specific examples of autoimmune diseases that can be treated or prevented with I and their pharmaceutical compns. include rheumatoid arthritis, systemic lupus erythematosis, and multiple sclerosis (no data).

REFERENCE COUNT: 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L27 ANSWER 6 OF 13 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2004:20322 CAPLUS

DOCUMENT NUMBER:

140:87658

DOCUMENT NUMBER

140:07030

TITLE:
INVENTOR(S):

Peptidomimetic modulators of cell adhesion

Gour, Barbara J.; Blaschuk, Orest W.; Ali, Anmar; Ni,

Feng; Chen, Zhigang; Michaud, Stephanie Denise; Wang,

Shaomeng; Hu, Zengjian

PATENT ASSIGNEE(S):

Can.

SOURCE:

U.S. Pat. Appl. Publ., 280 pp., Cont.-in-part of U.S.

Ser. No. 6,982.

CODEN: USXXCO

DOCUMENT TYPE:

Patent

LANGUAGE:

English

15

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004006011	A1	20040108	US 2003-425557	20030428
US 6031072	Α	20000229	US 1997-893534	19970711
US 6326352	B1	20011204	US 2000-507102	20000217
US 2002168761	A1	20021114	US 2001-769145	20010124
US 2002151475	A1	20021017	US 2001-6982	20011204
US 6914044	B2	20050705		
PRIORITY APPLN. INFO.:			US 1996-21612P	P 19960712
			US 1997-893534	A1 19970711
			US 2000-491078	B2 20000124
			US 2000-507102	A1 20000217
			US 2001-769145	B2 20010124
			US 2001-6982	A2 20011204

OTHER SOURCE(S): MARPAT 140:87658

AB Peptidomimetics of cyclic peptides, and compns. comprising such peptidomimetics are provided. The peptidomimetics have a three-dimensional structure that is substantially similar to a three-dimensional structure of a cyclic peptide that comprises a cadherin cell adhesion recognition sequence HAV. Methods for using such

peptidomimetics for modulating cadherin-mediated cell adhesion in a variety of contexts are also provided.

L27 ANSWER 7 OF 13 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER:

2003:737756 CAPLUS

DOCUMENT NUMBER:

139:261319

TITLE:

Preparation of 5-bromo-2,4-

pyrimidinediamines and related compounds as

cyclin dependent kinase inhibitors

INVENTOR (S):

Lucking, Ulrich; Krueger, Martin; Jautelat, Rolf;
Pries, Olaf: Siemeister, Gerd: Frast Alexander

Prien, Olaf; Siemeister, Gerd; Ernst, Alexander Schering Aktiengesellschaft, Germany

PATENT ASSIGNEE(S):

PCT Int. Appl., 116 pp.

SOURCE:

CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

German

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PA'	TENT :	NO.			KIN	D	DATE			APPL	ICAT:	ION I	NO.		D.	ATE	
						-									-		
WO	2003	0764	37		A1		2003	0918	,	WO 2	003-1	EP19	95		2	0030	226
	W:	ΑE,	AG,	ΑL,	AM,	AΤ,	ΑU,	AZ,	BA,	BB,	ВG,	BR,	BY,	ΒZ,	CA,	CH,	CN,
		CO,	CR,	CU,	CZ,	DK,	DM,	DZ,	EC,	EE,	ES,	FI,	GB,	GD,	GE,	GH,	GM,
		HR,	HU,	ID,	IL,	IN,	IS,	JP,	KE,	KG,	KΡ,	KR,	ΚZ,	LC,	LK,	LR.,	LS,
		LT,	LU,	LV,	MA,	MD,	MG,	MK,	MN,	MW,	MX,	MZ,	NO,	NZ,	OM,	PH,	PL,°
		PT,	RO,	RU,	sc,	SD,	SE,	SG,	SK,	SL,	ТJ,	TM,	TN,	TR,	TT,	TZ,	UA,
		UG,	UZ,	VC,	VN,	YU,	ZA,	ZM,	zw								
	RW:	GH,	GM,	KE,	LS,	MW,	MZ,	SD,	SL,	SZ,	TZ,	UG,	ZM,	ZW,	AM,	AZ,	BY,
		KG,	KZ,	MD,	RU,	TJ,	TM,	ΑT,	BE,	BG,	CH,	CY,	CZ,	DE,	DK,	EE,	ES,
		FI,	FR,	GB,	GR,	HU,	ΙE,	IT,	LU,	MC,	NL,	PT,	SE,	SI,	SK,	TR,	BF,
		ВJ,	CF,	CG,	CI,	CM,	GΑ,	GN,	GQ,	GW,	ML,	MR,	ΝE,	SN,	TD,	TG	
DE	1021	2100			A1		2003	1023		DE 2	002-1	1021	2100		2	0020	311
DE	1025	5984			A1		2004	0812		DE 2	002-1	1025	5984		2	0021	126
EP	1483	260			A1		2004	1208		EP 2	003-	7081	51		2	0030	226
	R:	AΤ,	BE,	CH,	DE,	DK,	ES,	FR,	GB,	GR,	IT,	LI,	LU,	NL,	SE,	MC,	PT,
		ΙE,	SI,	LT,	LV,	FI,	RO,	MK,	CY,	AL,	TR,	BG,	CZ,	EE,	HU,	SK	
US	2004	0637	37		A 1		2004	0401	1	US 2	003-3	3847	87		2	0031	027
PRIORIT	Y APP	LN.	INFO	.:					1	DE 2	002-3	1021	2100	I	A 2	0020	311
								•]	DE 2	002-3	1025	5984	I	A 20	0021	126
									1	US 2	002-3	3638	78P]	2 2	0020	314
									1	US 2	002-4	4300	53P	I	2 2	0021	202
									1	WO 2	003-1	EP19:	95	Ţ	V 2	0030	226
·OTHED CO		/al .			MAD	חאת	120.	2612	1.0								

OTHER SOURCE(S):

MARPAT 139:261319

GΙ

Title compds. I and II [D, E, G, L, M, T = C, O, N, S atom whereby at least a heteroatom must be contained in the ring; R1 = H, halo, alkyl, etc.; R2 = H, alkyl, alkenyl, etc.; A, B = H, OH, halo, etc.; n = 0, 1 with provisos] and their pharmaceutically acceptable salts were prepared For example, condensation of chloropyrimidine III, e.g., prepared from 5-bromo-2-chloro-4-hydroxypyrimidine in 2-steps, and threo-3-methylaminobutan-2-ol afforded pyrimidinediamine IV in 75% yield. In CDK2/CycE inhibition studies, 24-examples of compds. I exhibited IC50 values ranging from 6-74 nM. Compds. I are claimed useful as cardiovascular, antiviral, antitumor, etc. agents.

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L27 ANSWER 8 OF 13 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2003:133036 CAPLUS

DOCUMENT NUMBER: 138:180679

TITLE: SH3 protein domains and their ligands

INVENTOR(S): Booker, Grant William; Pyke, Simon Mathew; Branson,

Kim Mathew; Inglis, Steven Robert

PATENT ASSIGNEE(S): Adelaide Research & Innovation Pty Ltd., Australia

SOURCE: PCT Int. Appl., 176 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND D	DATE	APPLICATION NO.	DATE
WO 2003013523	A1 2	20030220	WO 2002-AU1064	20020808
W: AE, AG, AL,	AM, AT,	AU, AZ, BA,	BB, BG, BR, BY, BZ,	CA, CH, CN,
CO, CR, CU,	CZ, DE,	DK, DM, DZ,	EC, EE, ES, FI, GB,	GD, GE, GH,
GM, HR, HU,	ID, IL,	IN, IS, JP,	KE, KG, KP, KR, KZ,	LC, LK, LR,

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LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,
              PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ,
              UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD,
              RU, TJ, TM
          RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG,
              CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL,
              PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR,
              NE, SN, TD, TG
 PRIORITY APPLN. INFO.:
                                             AU 2001-6881
                                                                  A 20010808
 OTHER SOURCE(S):
                          MARPAT 138:180679
      The present invention relates generally to mols. capable of interaction
      with one or more domains within a proteinaceous mol. such as a peptide,
      polypeptide, protein or a macromol. comprising a proteinaceous mol. More
      particularly the present invention relates to mols. including ligands
      which are capable of interacting with, and more particularly, binding to,
      SH3 protein domains or homologs thereof and even more particularly to
      mols. including ligands which are capable of binding to SH3 domains having
      a three-dimensional ligand-binding site comprising a neg. charged residue
      and a hydrophobic residue linearly separated by at least five amino acid
      residues. The subject invention is preferably directed to the use of
      2-aminopyridine, 2-aminoquinoline, 1-aminoisoquinoline and derivs.,
      homologs, analogs and mimetics thereof or pharmaceutically acceptable
      salts thereof which interact with SH3 domains, and more particularly to
      the binding of 2-aminopyridine, 2-aminoquinoline, 1-aminoisoquinoline and
      derivs. analogs and mimetics to SH3 domains as defined above. The present
      invention contemplates the use of a three dimensional structure of the
      subject SH3 domain to identify, screen and design amino-substituted and
      amino-substituted pyridines and aminoquinolines capable of binding to an
      SH3 domain. The present invention is also useful for the in silico
      selection of derivs. homologs, analogs and mimetics of 2-aminopyridine,
      2-aminoquinoline, 1-aminoisoquinoline capable of binding to SH3 domains.
      The ligands of the present invention are useful in the development of a
      range of therapeutic and diagnostic agents.
REFERENCE COUNT:
                          2
                                THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS
                                RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT
 L27 ANSWER 9 OF 13 CAPLUS COPYRIGHT 2005 ACS on STN
 ACCESSION NUMBER:
                          2003:91269 CAPLUS
 DOCUMENT NUMBER:
                          139:62596
 TITLE:
                          Imidazopyrimidines, potent inhibitors of p38 MAP
                          Rupert, Kenneth C.; Henry, James R.; Dodd, John H.;
 AUTHOR (S):
                          Wadsworth, Scott A.; Cavender, Druie E.; Olini,
                          Gilbert C.; Fahmy, Bohumila; Siekierka, John J.
 CORPORATE SOURCE:
                          L.L.C., Drug Discovery, Johnson & Johnson
                          Pharmaceutical Research and Development, Raritan, NJ,
                          08869, USA
                          Bioorganic & Medicinal Chemistry Letters (2003),
 SOURCE:
                          13(3), 347-350
                          CODEN: BMCLE8; ISSN: 0960-894X
 PUBLISHER:
                          Elsevier Science Ltd.
 DOCUMENT TYPE:
                          Journal
 LANGUAGE:
                          English
 OTHER SOURCE(S):
                          CASREACT 139:62596
      The MAP kinase p38 is implicated in the release of the pro-inflammatory
      cytokines TNF-\alpha and IL-1\beta. Inhibition of cytokine release may
      be a useful treatment for inflammatory conditions such as
      rheumatoid arthritis and Crohn's disease. A novel
      series of imidazopyrimidines have been discovered that potently inhibit
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p38 and suppress the production of TNF- α in vivo.

IT 156-81-0, 2,4-Pyrimidinediamine

RL: RCT (Reactant); RACT (Reactant or reagent)

(imidazopyrimidines, potent inhibitors of p38 MAP kinase)

RN 156-81-0 CAPLUS

CN 2,4-Pyrimidinediamine (9CI) (CA INDEX NAME)

REFERENCE COUNT: 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L27 ANSWER 10 OF 13 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2002:449449 CAPLUS

DOCUMENT NUMBER: 137:33318

TITLE: Preparation of pyrimidinylaminothiazoles as tyrosine

kinase inhibitors.

INVENTOR(S): Bilodeau, Mark T.; Hartman, George D.; Hoffman, Jacob

M., Jr.; Lumma, William C., Jr.; Manley, Peter J.; Rodman, Leonard; Sisko, John T.; Smith, Anthony M.;

Tucker, Thomas J.

PATENT ASSIGNEE(S): Merck & Co., Inc., USA SOURCE: PCT Int. Appl., 169 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PAT	PATENT NO.															ATE	
									1	WO 2	2001-1	US44!	573		2	0011	130
WO	2002																
	W:										, BG,						
											, EE,						
		GM,	HR,	HU,	ID,	IL,	IN,	IS,	JP,	KE,	, KG,	KR,	ΚZ,	LC,	LK,	LR,	LS,
		LT,	LU,	LV,	MA,	MD,	MG,	MK,	MN,	MW,	, MX,	MZ,	NO,	ΝZ,	OM,	PH,	PL,
		PT,	RO,	RU,	SD,	SE,	SG,	SI,	SK,	SL	, TJ,	TM,	TR,	TT,	TZ,	UA,	UG,
		US,	UΖ,	VN,	YU,	ZA,	ZM,	ZW,	AM,	AZ,	, BY,	KG,	ΚZ,	MD,	RU,	ΤJ,	TM
	RW:	GH,	GM,	KE,	LS,	MW,	MZ,	SD,	SL,	SZ	, TZ,	UG,	ZM,	ZW,	ΑT,	BE,	CH,
		CY,	DE,	DK,	ES,	FI,	FR,	GB,	GR,	IE,	, IT,	LU,	MC,	NL,	PT,	SE,	TR,
		BF,	ВJ,	CF,	CG,	CI,	CM,	GA,	GN,	GQ.	, GW,	ML,	MR,	ΝE,	SN,	TD,	TG
US	2002	1377	55		A1		2002	0926		US 2	2001-	9904	73		2	0011	121
	2429										2001-						
AU	2002	0324	41		A5		2002	0618		AU 2	2002-	3244	1		2	0011	130
	1341										2001-						
	R:										, IT,						
		IE.	SI.	LT.	LV,	FI,	RO,	MK,	CY,	AL	, TR						
JР	IE, SI, L' JP 2004524282						2004	0812		JP :	2002-	5474	38		2	0011	130
US	US 2004524282						2004	0401		US :	2003-	6776	87		2	0031	
	RIORITY APPLN. INFO.:									US :	2000-	2510	06P		P 2	0001	204
	RIORITI MILLINI IMIOI.									US :	2001-	9904	73		A1 2	0011	121
										WO :	2001-	US44	573	1	W 2	0011	130
OMITTED OF	aman.		MAD	יייעם	127.	2221	Ω										

OTHER SOURCE(S): MARPAT 137:33318

GI

AB Title compds. [I; A, B = N, NO; Y = O, S, NR4; R1, R2 = H, perfluoroalkoxy, OH, cyano, halo, (substituted) alkyl(oxy) (carbonyl), aryl(oxy) (carbonyl), heterocyclyl, etc.; R4 = H, aryl, alkyl; R5 = H, SO2Rc, CORc, Rc, CO2Rc; R6 = aryl, cyano, halo, (substituted) alkyl, alkenyl, alkynyl, heterocyclyl, aminocarbonyl; Rc = alkyl, aryl, heterocyclyl], were prepared for treating angiogenesis, cancer, tumor growth, atherosclerosis, age related macular degeneration, diabetic retinopathy, inflammation, etc. Thus, 4-aminopyrimidine was stirred with NaH in THF; 2-bromo-5-phenylthiazole was added and the mixture was refluxed overnight to give 5-phenylthiazol-2-yl pyrimidin-4-yl amine. I inhibited vascular endothelial growth factor-stimulated mitogenesis of human vascular endothelial cells with IC50 = 0.01-5.0 nM.

IT 156-81-0, 2,4-Diaminopyrimidine

RL: RCT (Reactant); RACT (Reactant or reagent)

(preparation of pyrimidinylaminothiazoles as tyrosine kinase inhibitors)

RN 156-81-0 CAPLUS

CN 2,4-Pyrimidinediamine (9CI) (CA INDEX NAME)

L27 ANSWER 11 OF 13 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2002:869496 CAPLUS

DOCUMENT NUMBER: 1

137:363033

TITLE:

Peptidomimetic modulators of cell adhesion

INVENTOR(S):

Gour, Barbara J.; Blaschuk, Orest W.; Ali, Anmar; Ni,

Feng; Chen, Zhigang; Michaud, Stephanie D.; Wang,

Shoameng; Hu, Zenjian

PATENT ASSIGNEE(S):

Can.

SOURCE:

U.S. Pat. Appl. Publ., 309 pp., Cont.-in-part of U.S.

Ser. No. 491,078.

CODEN: USXXCO

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT: 15

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2002168761	A1	20021114	US 2001-769145	20010124
US 2004058864	A1	20040325	US 2003-412701	20030410
US 2004006011	A1	20040108	US 2003-425557	20030428
PRIORITY APPLN. INFO.:			US 2000-491078	A2 20000124
			US 1996-21612P	P 19960712
			US 1997-893534	A1 19970711

US 2000-507102 A1 20000217 B1 20010124 US 2001-769145 US 2001-6982 A2 20011204

OTHER SOURCE(S): MARPAT 137:363033

Peptidomimetics of cyclic peptides, and compns. comprising such peptidomimetics are provided. The peptidomimetics have a three-dimensional structure that is substantially similar to a three-dimensional structure of a cyclic peptide that comprises a cadherin cell adhesion recognition sequence HAV. Methods for using such peptidomimetics for modulating cadherin-mediated cell adhesion in a variety of contexts are also provided.

L27 ANSWER 12 OF 13 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER:

2000:457043 CAPLUS

DOCUMENT NUMBER:

133:89537

TITLE:

Preparation of 2,4-

pyrimidinediamine derivatives as anticancer

agents

INVENTOR(S):

Bradbury, Robert Hugh; Breault, Gloria Anne; Jewsbury,

Philip John; Pease, Janet Elizabeth

PATENT ASSIGNEE(S):

Astrazeneca UK Limited, UK

SOURCE:

PCT Int. Appl., 137 pp.

CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

P	ATENT															ATE	
- W	 0 2000										1999-					9991:	220
	W:	ΑE,	AL,	AM,	ΑT,	AU,	, AZ,	BA,	BB,	ВĢ	, BR,	BY,	CA,	CH,	CN,	CR,	CU,
		CZ.	DE,	DK,	DM,	EE.	ES,	FI,	GB,	GD	, GE,	GH,	GM,	HR,	HU,	ID,	IL,
		IN.	ıs.	JP.	KE,	KG	KP,	KR,	ΚŻ,	LC	, LK,	LR,	LS,	LT,	LU,	LV,	MA,
		MD.	MG.	MK.	MN,	MW	, MX,	NO,	NZ,	ΡL	, PT,	RO,	RU,	SD,	SE,	SG,	SI,
		sĸ.	SL.	TJ.	TM.	TR	TT.	TZ,	UA,	UG	, US,	UZ,	VN,	YU,	ZA,	ZW,	AM,
		•		•	•		RU.	•	•			•	•	•	•	•	•
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		DK,	ES,	FI.	FR,	GB	GR,	IE,	IT,	LU	, MC,	NL,	PT,	SE,	BF,	ВJ,	CF,
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B:	R 9916	590			Α		2001	1023		BR	1999-	1659	0		1	9991:	220
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A ¹	U 7630	91 🕶			B2		2003	0710		AU	2000-	1874	3		1.	9991:	220
N.	Z 5121	18-					2003	0829		NZ	1999-	5121	18		1.	9991:	220
A'	Г 2770	20			E		2004	1015		\mathtt{AT}	1999-	9623	75		1	9991	220
	S 2228				Т3		2005				1999-						
Z	A 2001	0044	13		Α		2002	0829		ZA	2001-	4413			2	0010	529
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U	S 6593	326		B1		2003	0715		US	2001-	8686	02		2	0010	823	
PRIORI'	TY APP	.:						GB	1998-	2851	1	Ž	A 1	9981	224		
										WO	1999-	GB43	25	1	<i>N</i> 1	9991:	220
OTHER :	SOURCE	(S):			MAR	TAG	133:	8953	7								

GΙ

The present invention relates to the title compds. (I) [wherein R1 = H, AB (un) substituted alkyl, alkenyl, or alkynyl, benzyl, 2-phenylethyl, phthalimidoalkyl, or cycloalkylalkyl; Rx = halo, OH, NO2, NH2, CN, SH, CO2H, SO2NH2, NHCHO, ureido, etc.; Q1 and Q2 = independently (un) substituted aryl, 5- or 6-membered monocycle, or 9- or 10-membered bicyclic heterocycle], processes for their manufacture, and pharmaceutical compns. containing them. For example, addition of 4-[2-hydroxy-3-(N,Ndimethylamino)propoxy]aniline.HCl in MeOH to 5-bromo-2-chloro-4-(indan-5-ylamino)pyrimidine in BuOH (prepns. given) and heating to 100°C for 18 h gave II (42%). I inhibited the effects of cylin-dependent serine/threonine kinases (CDKs), showing selectivity for CDK2 (no data), CDK4 (IC50 ranging from 0.02 μM to 0.07 μM), and CDK6 (no data). In a tyrosine kinase activity assay using Sf21 cells transfected with plaque-pure FAK recombinant virus, I also inhibited focal adhesion kinase 3 (FAK3) with IC50 ranging from 0.032 μ M to 0.07 μ M. Typical IC50 values for I when tested for inhibition of cell growth in an Sulforhodamine B (SRB) assay were in the range of 1 mM to 1 nM. possess anti-cancer properties, including anti-cell-migration, antiproliferation and/or apoptotic properties. Such properties are expected to be of value in the treatment of disease states associated with aberrant cell cycles and cell proliferation such as cancers (solid tumors and leukemias), fibroproliferative and differentiative disorders, psoriasis, rheumatoid arthritis, Kaposi's sarcoma, hemangioma, acute and chronic nephropathies, atheroma, atherosclerosis, arterial restenosis, autoimmune diseases, acute and chronic inflammation, bone diseases, and ocular diseases with retinal vessel proliferation.

II

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L27 ANSWER 13 OF 13 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED. on STN

ACCESSION NUMBER: 91081327 EMBASE

DOCUMENT NUMBER: 1991081327

TITLE: Therapy of acute and chronic multiple

sclerosis.

AUTHOR: Tindall R.S.A.

CORPORATE SOURCE: Department of Neurology, University of Southern California,

Los Angeles Veterans Administration Facility, 425 South

Hill Street, Los Angeles, CA 90013, United States

SOURCE: Comprehensive Therapy, (1991) Vol. 17, No. 1, pp. 18-25.

ISSN: 0098-8243 CODEN: COTHD3

COUNTRY: United States
DOCUMENT TYPE: Journal; Article

Page 20

Neurology and Neurosurgery 800 FILE SEGMENT: Immunology, Serology and Transplantation 026 037 Drug Literature Index English LANGUAGE: Entered STN: 911216 ENTRY DATE: Last Updated on STN: 911216 DATA NOT AVAILABLE FOR THIS ACCESSION NUMBER => s singh r?/au;s argade a?/au;s payan d?/au 2983 FILE MEDLINE L28 L29 7931 FILE BIOSIS 2556 FILE EMBASE L30 9987 FILE CAPLUS L31 TOTAL FOR ALL FILES 23457 SINGH R?/AU L32 1 FILE MEDLINE L33 8 FILE BIOSIS L347 FILE EMBASE L35 21 FILE CAPLUS L36 TOTAL FOR ALL FILES L37 37 ARGADE A?/AU 144 FILE MEDLINE L38 206 FILE BIOSIS L39 138 FILE EMBASE L40158 FILE CAPLUS L41TOTAL FOR ALL FILES 646 PAYAN D?/AU L42=> s 132 and 137 and 142 O FILE MEDLINE L43 1 FILE BIOSIS L44 O FILE EMBASE L45 2 FILE CAPLUS L46 TOTAL FOR ALL FILES 3 L32 AND L37 AND L42 L47 => s 147 not 126 O FILE MEDLINE L481 FILE BIOSIS L49 O FILE EMBASE L50 1 FILE CAPLUS L51 TOTAL FOR ALL FILES 2 L47 NOT L26 L52 => dup rem 152 PROCESSING COMPLETED FOR L52 2 DUP REM L52 (0 DUPLICATES REMOVED) L53

Prepared by: Mary Hale @2-2507 Rem Bldg 1D86

=> d ibib abs 1-2

L53 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER:

2003:610204 CAPLUS

DOCUMENT NUMBER:

139:164801

TITLE:

Preparation of 2,4-pyrimidinediamines as IgE and/or IgG receptor modulators for treatment of allergic diseases, inflammatory conditions, and tissue

destruction

INVENTOR (S):

Singh, Rajinder; Argade, Ankush;

Payan, Donald G.; Molineaux, Susan; Holland,

Sacha J.; Clough, Jeffrey; Keim, Holger; Bhamidipati, Somasekhar; Sylvain, Catherine; Li, Weigun; Rossi,

Alexander B.

PATENT ASSIGNEE(S):

Rigel Pharmaceuticals, Inc., USA

SOURCE:

PCT Int. Appl., 648 pp.

DOCUMENT TYPE:

CODEN: PIXXD2 Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION: חא ייינאייי או

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	JP	2005	5160	46		T2		2005	0602		JP 2	003-	5634	90		2	0030	131
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										•	US 2	002-3	3996	73P]	P 2	0020	729
										1	US 2	002-4	4342	77P]	P 2	0021	217
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OTHER SOURCE(S):

MARPAT 139:164801

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Title compds. I [wherein L1 and L2 = independently a bond or a linker; R2 = (un) substituted alkyl, (hetero) cycloalkyl, or (hetero) aryl; R4 = H or R2; R5 = R6 or (un) substituted alkyl, alkenyl, or alkynyl; R6 = independently H, an electroneg. group, protected alc. or thiol, haloalkyl(oxy), halo, CN, NC, OCN, SCN, NO, NO2, N3, or (un) substituted amino, sulfamoyl(oxy), acyl, carboxy, carbamoyl, (hetero)aryl(alkyl), etc.; with provisos and exclusions; and salts, hydrates, solvates, N-oxides, and prodrugs thereof] were prepared as inhibitors of the IgE and/or IgG receptor signaling cascades that lead to the release of chemical mediators. For example, coupling of 2,4-dichloropyrimidine with 4-ethoxyaniline in EtOH provided N2,N4-bis(4-ethoxyphenyl)-2,4pyrimidinediamine (II). The latter inhibited degranulation of bone marrow derived mast cells challenged with anti-IgE and ionomycin with IC50 values of 4.5 μM and 4.4 $\mu M,$ resp. Thus, I and their pharmaceutical compns. are useful in the treatment and prevention of diseases characterized by, caused by, or associated with the release of chemical mediators via degranulation of mast, basophil, neutrophil, or eosinophil cells and other processes effected by activation of the IgE and/or IgG receptor signaling cascades. The treatment and prevention of allergic diseases, low grade scarring, diseases associated with tissue destruction, diseases associated with tissue inflammation, inflammation, and scarring are targeted uses (no data).

ΙI

L53 ANSWER 2 OF 2 ACCESSION NUMBER:

BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN 2002:165568 BIOSIS

DOCUMENT NUMBER: TITLE:

AUTHOR (S):

PREV200200165568 Development and utilization of cultured human mast cells

for high throughput small molecule drug discovery.

Rossi, Alexander [Reprint author]; Holland, Sacha [Reprint

author]; Woronicz, John [Reprint author]; Quast, Jeff

[Reprint author]; Argade, Ankush; Sylvain,

Catherine; Juencke, Sara; Sula, Caroline; Tombo, Wendy

[Reprint author]; Goodrich, Bethany; Pine, Polly;

Scheerens, Heleen; Natarajan, Gita; Li, Wenbao; Bennett, Mark [Reprint author]; Daniel, Ruby; Wagner, Gregory; Singh, Rajinder; Molineaux, Susan [Reprint author];

Payan, Donald

CORPORATE SOURCE:

Cell Biology, Rigel Pharmaceuticals, Inc., 240 East Grand

Avenue, So. San Francisco, CA, 94080, USA

Molecular Biology of the Cell, (Nov, 2001) Vol. 12, No. SOURCE: Supplement, pp. 512a-513a. print.

Meeting Info.: 41st Annual Meeting of the American Society

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for Cell Biology. Washington DC, USA. December 08-12, 2001.
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American Society for Cell Biology. CODEN: MBCEEV. ISSN: 1059-1524.

DOCUMENT TYPE:

Conference; (Meeting)

Conference; Abstract; (Meeting Abstract)

LANGUAGE:

English

ENTRY DATE:

Entered STN: 5 Mar 2002

Last Updated on STN: 5 Mar 2002

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=> s keim h?/au;s bhamidipati s?/au;s sylvain c?/au;s li h?/au
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L54 84 FILE MEDLINE L55 57 FILE BIOSIS L56 57 FILE EMBASE L57 70 FILE CAPLUS

TOTAL FOR ALL FILES

L58 268 KEIM H?/AU

L59 8 FILE MEDLINE
L60 18 FILE BIOSIS
L61 7 FILE EMBASE
L62 16 FILE CAPLUS

TOTAL FOR ALL FILES

L63 49 BHAMIDIPATI S?/AU

L64 8 FILE MEDLINE L65 13 FILE BIOSIS L66 11 FILE EMBASE L67 10 FILE CAPLUS

TOTAL FOR ALL FILES

L68 42 SYLVAIN C?/AU

L69 5342 FILE MEDLINE L70 6316 FILE BIOSIS L71 4069 FILE EMBASE L72 21181 FILE CAPLUS

TOTAL FOR ALL FILES

L73 36908 LI H?/AU

=> s 158 and 163 and 168 and 173

L74 0 FILE MEDLINE
L75 0 FILE BIOSIS
L76 0 FILE EMBASE
L77 3 FILE CAPLUS

TOTAL FOR ALL FILES

L78 3 L58 AND L63 AND L68 AND L73

=> s 178 not 152

L79 0 FILE MEDLINE
L80 0 FILE BIOSIS
L81 0 FILE EMBASE
L82 3 FILE CAPLUS

TOTAL FOR ALL FILES

L83 3 L78 NOT L52

=> d 1-3 ibib abs

INVENTOR (S):

L83 ANSWER 1 OF 3 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2005:158646 CAPLUS

DOCUMENT NUMBER: 142:254587

TITLE: Methods for treating or preventing autoimmune diseases

with 2,4-pyrimidinediamine compounds
Rajinder, Singh; Ankush, Argade; Li, Hui;
Bhamidipati, Somasekhar; Carroll, David;

Sylvain, Catherine; Clough, Jeffrey;

Keim, Holger

PATENT ASSIGNEE(S): Rigel Pharmaceuticals, Inc., USA

SOURCE: PCT Int. Appl., 276 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 3

PATENT INFORMATION:

PA.	PATENT NO.						KIND DATE			APPL	ICAT		DATE					
WO	WO 2005016893						A2 20050224			WO 2	 004-1		20040730					
WO	2005	0168		A3 20050			0609	09										
	W:	ΑE,	AG,	AL,	AM,	ΑT,	AU,	AZ,	BA,	BB,	BG,	BR,	BW,	BY,	ΒZ,	CA,	CH,	
		CN,	CO,	CR,	CU,	CZ,	DE,	DK,	DM,	DZ,	EC,	EE,	EG,	ES,	FI,	GB,	GD,	
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		ΑZ,	BY,	KG,	KΖ,	MD,	RU,	ТJ,	TM,	ΑT,	BE,	BG,	CH,	CY,	CZ,	DE,	DK,	
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PRIORITY	PRIORITY APPLN. INFO.:								7	US 2	003-	4916	41P]	P 20	0030	730	
					US 2003-53159						98P	P P 20031219						

OTHER SOURCE(S): MARPAT 142:254587

AB The invention provides methods for treating or preventing autoimmune diseases with 2,4-pyrimidinediamine compds., as well as methods of treating, preventing or ameliorating symptoms associated with such diseases. Specific examples of autoimmune diseases that can be treated or prevented with the compds. include rheumatoid arthritis and/or its associated symptoms, systemic lupus erythematosis and/or its associated symptoms and multiple sclerosis and/or its associated symptoms.

L83 ANSWER 2 OF 3 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2005:120923 CAPLUS

DOCUMENT NUMBER: 142:219300

TITLE: 2,4-Pyrimidinediamines for use in the treatment or

prevention of autoimmune diseases

INVENTOR(S): Rajinder, Singh; Ankush, Argade; Li, Hui;

Bhamidipati, Somasekhar; Carroll, David; Sylvain, Catherine; Clough, Jeffrey;

US 2004-572246P

P 20040518

Keim, Holger

PATENT ASSIGNEE(S): Rigel Pharmaceuticals, Inc., USA

SOURCE:

PCT Int. Appl., 169 pp.

CODEN: PIXXD2

DOCUMENT TYPE:

Patent English

LANGUAGE:

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FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PATENT NO.						KIND DATE			1	APPL	ICAT:	ION I	DATE				
									- -			*					
W	A1 20050210			1	WO 20	004-1	JS24		20040730								
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		CN,	CO,	CR,	CU,	CZ,	DE,	DK,	DM,	DZ,	EC,	EE,	EG,	ES,	FI,	GB,	GD,
		GE,	GH,	GM,	HR,	HU,	ID,	IL,	IN,	IS,	JP,	KE,	KG,	ΚP,	KR,	KZ,	LC,
								MA,									
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	RW:	BW,	GH,	GM,	KE,	LS,	MW,	MZ,	NA,	SD,	SL,	SZ,	TZ,	UG,	ZM,	ZW,	AM,
		AZ,	BY,	KG,	KZ,	MD,	RU,	ТJ,	TM,	ΑT,	BE,	BG,	CH,	CY,	CZ,	DE,	DK,
								HU,									
		SI,	SK,	TR,	BF,	ВJ,	CF,	CG,	CI,	CM,	GA,	GN,	GQ,	GW,	ML,	MR,	NE,
		SN,	·TD,	TG													
PRIORITY APPLN. INFO.:										US 2	003-	4916		P 20030730			
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									•	US 2	004-	5722	46P		P 2	0040	518
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OTHER SOURCE(S):

MARPAT 142:219300

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$$\begin{array}{c|c}
 & R6 \\
 & N \\
 & N$$

The present invention provides methods of treating or preventing autoimmune diseases with 2,4-pyrimidinediamine compds. I [L1, L2 = a direct bond or a linker; R2 = II; R4 = III; X = N, CH; Y, Z = O, S, SO, SO2, etc.; R5 = R6, alkyl, alkenyl, etc.; R6 = H, an electroneg. group, alkoxy, haloalkoxy, etc.; R31 = Me, alkyl; R35 = H, alkyl, cycloalkyl, etc.; or two R35 bonded together to the same carbon atom are taken together to form an oxo, (un) substituted NH], as well as methods of treating, preventing or ameliorating symptoms associated with such diseases. Specific examples of autoimmune diseases that can be treated or prevented with the compds. I include rheumatoid arthritis and/or its associated symptoms, systemic lupus erythematosus and/or its associated symptoms and multiple sclerosis and/or its associated symptoms. The general procedures

for synthesis of compds. I are described. The characterization data for over 500 prepared compds. I were given in table. The compds. I were tested in various tests (e.g., inhibition of IgE-induced degranulation, inhibition of Syk kinase, etc.). For example, N4-(2,2-dimethyl-3-oxo-4H-5-pyrido[1,4]oxazin-6-yl)-5-fluoro-N2-(3,4,5-trimethoxyphenyl)-2,4-pyrimidinediamine showed 99.8% inhibition of edema formation when administered at 5 mg/kg in mice.

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L83 ANSWER 3 OF 3 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2004:142963 CAPLUS

DOCUMENT NUMBER: 140:199334

TITLE: Preparation of 2,4-pyrimidinediamines as IgE and/or

IgG receptor modulators for treatment of autoimmune

diseases

INVENTOR(S): Singh, Rajinder; Argade, Ankush; Payan, Donald G.;

Clough, Jeffrey; Keim, Holger; Sylvain,

Catherine; Li, Hui; Bhamidipati,

Somasekhar

PATENT ASSIGNEE(S): Rigel Pharmaceuticals, USA SOURCE: PCT Int. Appl., 811 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

I	PATENT NO.							IND DATE APPLICATION NO.								DATE				
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OTHER SOURCE(S): MARPAT 140:199334

GΙ

AΒ The present invention provides methods of treating or preventing autoimmune diseases with 2,4-pyrimidinediamine compds., as well as methods of treating, preventing or ameliorating symptoms associated with such diseases. Title compds. I [wherein L1 and L2 = independently a bond or a linker; R2 = (un)substituted alkyl, (hetero)cycloalkyl, or (hetero)aryl; R4 = H or R2; R5 = R6 or (un)substituted alkyl, alkenyl, or alkynyl; R6 = independently H, an electroneg. group, protected alc. or thiol, haloalkyl(oxy), halo, CN, NC, OCN, SCN, NO, NO2, N3, or (un)substituted amino, sulfamoyl(oxy), acyl, carboxy, carbamoyl, (hetero)aryl(alkyl), etc.; with provisos and exclusions; and salts, hydrates, solvates, N-oxides, and prodrugs thereof] were prepared as inhibitors of the IgE and/or IgG receptor signaling cascades that lead to the release of chemical mediators. For example, coupling of 2,4-dichloropyrimidine with 4-ethoxyaniline in EtOH provided N2,N4-bis(4-ethoxyphenyl)-2,4pyrimidinediamine (II). The latter inhibited degranulation of bone marrow derived mast cells challenged with anti-IgE and ionomycin with IC50 values of 4.5 μM and 4.4 μM , resp. Thus, I and their pharmaceutical compns. are useful in the treatment and prevention of diseases characterized by, caused by, or associated with the release of chemical mediators via degranulation of mast, basophil, neutrophil, or eosinophil cells and other processes effected by activation of the IgE and/or IgG receptor signaling cascades. Specific examples of autoimmune diseases that can be treated or prevented with I and their pharmaceutical compns. include rheumatoid arthritis, systemic lupus erythematosis, and multiple sclerosis (no data).

REFERENCE COUNT:

THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> dis his

(FILE 'HOME' ENTERED AT 10:15:21 ON 17 AUG 2005)

12

FILE 'REGISTRY' ENTERED AT 10:15:38 ON 17 AUG 2005

E "2,4-PYRIMIDINEDIAMINE"/CN 5

L1 1 S E3

E "R 921302"/CN 5

E "R921302"/CN 5

E "R 926891"/CN 5

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E "R926891"/CN 5
                E "R 940323"/CN 5
                E "R940323"/CN 5
                E "R 940347"/CN 5
                E "R940347"/CN 5
                E "R 921303"/CN 5
                E "R921303"/CN 5
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L2
         136215 FILE MEDLINE
         119817 FILE BIOSIS
L3
L4
         136957 FILE EMBASE
         60193 FILE CAPLUS
L5
     TOTAL FOR ALL FILES
        453182 S (AUTOIMMUNE DISEASE OR AUTOIMMUNE ENCEPHALOMYELIT? OR RHEUMAT
L6
L7
              O FILE MEDLINE
L8
              0 FILE BIOSIS
L9
              O FILE EMBASE
         250623 FILE MEDLINE
L10
L11
         50150 FILE BIOSIS
L12
              O FILE EMBASE
              O FILE CAPLUS
L13
     TOTAL FOR ALL FILES
       300773 S C20.111?/CT
L14
             39 FILE MEDLINE
L15
             62 FILE BIOSIS
L16
L17
             35 FILE EMBASE
L18
           351 FILE CAPLUS
     TOTAL FOR ALL FILES
L19
           487 S L1 OR "2,4-PYRIMIDINEDIAMINE" OR "2,4-DIAMINOPYRIDINE" OR NSC
L20
             39 FILE MEDLINE
L21
             62 FILE BIOSIS
L22
              O FILE MEDLINE
L23
              O FILE BIOSIS
L24
              1 FILE EMBASE
L25
             12 FILE CAPLUS
     TOTAL FOR ALL FILES
             13 S L19 AND (L6 OR L14)
L26
L27
             13 DUP REM L26 (0 DUPLICATES REMOVED)
L28
           2983 FILE MEDLINE
           7931 FILE BIOSIS
L29
L30
           2556 FILE EMBASE
L31
           9987 FILE CAPLUS
     TOTAL FOR ALL FILES
         23457 S SINGH R?/AU
L32
L33
              1 FILE MEDLINE
L34
              8 FILE BIOSIS
L35
              7 FILE EMBASE
L36
             21 FILE CAPLUS
     TOTAL FOR ALL FILES
L37
             37 S ARGADE A?/AU
            144 FILE MEDLINE
L38
            206 FILE BIOSIS
L39
            138 FILE EMBASE
L40
L41
           158 FILE CAPLUS
     TOTAL FOR ALL FILES
L42
            646 S PAYAN D?/AU
L43
              O FILE MEDLINE
L44
              1 FILE BIOSIS
              O FILE EMBASE
L45
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Page 29
```

```
2 FILE CAPLUS
L46
     TOTAL FOR ALL FILES
             3 S L32 AND L37 AND L42
L47
             O FILE MEDLINE
L48
L49
             1 FILE BIOSIS
L50
             O FILE EMBASE
             1 FILE CAPLUS
L51
    TOTAL FOR ALL FILES
            2 S L47 NOT L26
L52
             2 DUP REM L52 (0 DUPLICATES REMOVED)
L53
L54
            84 FILE MEDLINE
            57 FILE BIOSIS
L55
            57 FILE EMBASE
L56
            70 FILE CAPLUS
L57
    TOTAL FOR ALL FILES
    268 S KEIM H?/AU
L58
L59
            8 FILE MEDLINE
            18 FILE BIOSIS
L60
             7 FILE EMBASE
L61
           16 FILE CAPLUS
L62
     TOTAL FOR ALL FILES
     49 S BHAMIDIPATI S?/AU
L63
            8 FILE MEDLINE
L64
L65
            13 FILE BIOSIS
            11 FILE EMBASE
L66
            10 FILE CAPLUS
L67
    TOTAL FOR ALL FILES
           42 S SYLVAIN C?/AU
L68
L69
          5342 FILE MEDLINE
          6316 FILE BIOSIS
L70
L71
          4069 FILE EMBASE
L72
         21181 FILE CAPLUS
     TOTAL FOR ALL FILES
L73 36908 S LI H?/AU
L74
             O FILE MEDLINE
L75
             0 FILE BIOSIS
L76
             O FILE EMBASE
L77
             3 FILE CAPLUS
    TOTAL FOR ALL FILES
L78
     3 S L58 AND L63 AND L68 AND L73
L79
             O FILE MEDLINE
L80
             0 FILE BIOSIS
L81
             0 FILE EMBASE
L82
             3 FILE CAPLUS
    TOTAL FOR ALL FILES
L83
             3 S L78 NOT L52
=> log y
COST IN U.S. DOLLARS
                                               SINCE FILE
                                                    FILE TOTAL SESSION
                                                              TOTAL
FULL ESTIMATED COST
                                                   138.76
                                                            146.93
DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)
                                               SINCE FILE
                                                  CE FILE
ENTRY
                                                             TOTAL
                                                            SESSION
                                                   -11.68
CA SUBSCRIBER PRICE
                                                            -11.68
```

STN INTERNATIONAL LOGOFF AT 10:26:10 ON 17 AUG 2005



=> fil reg COST IN U.S. DOLLARS

SINCE FILE TOTAL ENTRY SESSION 0.21 0.21

FULL ESTIMATED COST

FILE 'REGISTRY' ENTERED AT 10:15:38 ON 17 AUG 2005 USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT. PLEASE SEE "HELP USAGETERMS" FOR DETAILS. COPYRIGHT (C) 2005 American Chemical Society (ACS)

Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 16 AUG 2005 HIGHEST RN 860495-66-5 DICTIONARY FILE UPDATES: 16 AUG 2005 HIGHEST RN 860495-66-5

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH JANUARY 18, 2005

Please note that search-term pricing does apply when conducting SmartSELECT searches.

Structure search iteration limits have been increased. See HELP SLIMITS for details.

Experimental and calculated property data are now available. For more information enter HELP PROP at an arrow prompt in the file or refer to the file summary sheet on the web at: http://www.cas.org/ONLINE/DBSS/registryss.html

```
=> e "2,4-pyrimidinediamine"/cn 5
E1
                   2,4-PYRIMIDINEDIACETONITRILE, 6-AMINO-5-CYANO-A2-(PHEN
             1
                   YLMETHYLENE) -/CN
E2
                   2,4-PYRIMIDINEDIACETONITRILE, 6-AMINO-5-CYANO-A4-((3-C
                   YANO-4,5,6,7-TETRAHYDROBENZO(B)THIEN-2-YL)HYDRAZONO)-/CN
             1 --> 2,4-PYRIMIDINEDIAMINE/CN
E3
                   2,4-PYRIMIDINEDIAMINE, 1,2-DIHYDRO-N,N'-BIS(4-METHYLPHENYL)-
E4
                   1-NITRO-/CN
E5
             1
                   2,4-PYRIMIDINEDIAMINE, 1,4-DIHYDRO-N2,N2-DIMETHYL-, ION(1-)/
                   CN
```

=> s e3;d ide can L1 1 "2,4-PYRIMIDINEDIAMINE"/CN

```
L1 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2005 ACS on STN
```

RN 156-81-0 REGISTRY

ED Entered STN: 16 Nov 1984

CN 2,4-Pyrimidinediamine (9CI) (CA INDEX NAME)

```
Page 2
```

OTHER CA INDEX NAMES: Pyrimidine, 2,4-diamino- (6CI, 7CI, 8CI) OTHER NAMES: 2,4-Diaminopyrimidine NSC 30856 3D CONCORD FS 42910-88-3, 42910-89-4, 42910-90-7, 42910-92-9 DR MF CI STN Files: AGRICOLA, ANABSTR, BEILSTEIN*, BIOBUSINESS, BIOSIS, CA, LCCANCERLIT, CAOLD, CAPLUS, CASREACT, CHEMCATS, CHEMLIST, CSCHEM, EMBASE, MEDLINE, SPECINFO, TOXCENTER, USPAT2, USPATFULL (*File contains numerically searchable property data) Other Sources: EINECS** (**Enter CHEMLIST File for up-to-date regulatory information)

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

254 REFERENCES IN FILE CA (1907 TO DATE)
44 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
254 REFERENCES IN FILE CAPLUS (1907 TO DATE)
7 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

REFERENCE 1: 143:138607

REFERENCE 2: 143:72294

REFERENCE 3: 142:254587

REFERENCE 4: 142:212327

REFERENCE 5: 142:74474

REFERENCE 6: 142:38288

REFERENCE 7: 141:260782

REFERENCE 8: 141:93976

REFERENCE 9: 141:76686

REFERENCE 10: 141:76353

=> e "r 921302"/cn 5

E1 1 R 91650/CN E2 1 R 920K/CN E3 0 --> R 921302/CN E4 1 R 922/CN E5 1 R 922-1/CN

=> e "r921302"/cn 5

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Page 3
                    R9 STEEL/CN
E1
              1
                    R900/CN
E2
              1
              0 --> R921302/CN
E3
E4
              1
                    R9F4K5/CN
E5
              1
                    R9F5/CN
=> e "r 926891"/cn 5
E1
             1
                    R 925SH3/CN
                    R 92625/CN
E2
              1
              0 --> R 926891/CN
E3
E4
                   R 9298/CN
             1
E5
             3
                    R 930/CN
=> e "r926891"/cn 5
                    R9 STEEL/CN
E1
             1
                    R900/CN
E2
              1
E3
              0
               --> R926891/CN
                    R9F4K5/CN
E4
             1
E5
              1
                    R9F5/CN
=> e "r 940323"/cn 5
                    R 9403/CN
E1
             1
E2
             1
                    R 9403, HOMOPOLYMER/CN
E3
             0 --> R 940323/CN
E4
                    R 94138/CN
             1
E5
             1
                    R 9422/CN
=> e "r940323"/cn 5
E1
             1
                    R9 STEEL/CN
                    R900/CN
E2
             1
               --> R940323/CN
E3
             0
                    R9F4K5/CN
E4
             1
E5
             1
                    R9F5/CN
=> e "r 940347"/cn 5
                    R 9403/CN
E1
             1
E2
             1
                    R 9403, HOMOPOLYMER/CN
E3
             0 --> R 940347/CN
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             1
                    R 94138/CN
E5
             1
                    R 9422/CN
=> e "r940347"/cn 5
                    R9 STEEL/CN
E1
             1
E2
             1
                    R900/CN
E3
             0
               --> R940347/CN
E4
             1
                    R9F4K5/CN
E5
             1
                    R9F5/CN
=> e "r 921303"/cn 5
                    R 91650/CN
E1
             1
E2
             1
                   R 920K/CN
E3
             0 --> R 921303/CN
E4
             1
                   R 922/CN
E5
             1
                    R 922-1/CN
=> e "r921303"/cn 5
E1
             1
                   R9 STEEL/CN
E2
             1
                   R900/CN
E3
             0 --> R921303/CN
E4
             1
                    R9F4K5/CN
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E5 1 R9F5/CN

=> fil medl,biosis,embase,caplus
COST IN U.S. DOLLARS

FULL ESTIMATED COST ENTRY SESSION 7.96 8.17

FILE 'MEDLINE' ENTERED AT 10:17:20 ON 17 AUG 2005

FILE 'BIOSIS' ENTERED AT 10:17:20 ON 17 AUG 2005 Copyright (c) 2005 The Thomson Corporation

FILE 'EMBASE' ENTERED AT 10:17:20 ON 17 AUG 2005 COPYRIGHT (C) 2005 Elsevier Inc. All rights reserved.

FILE 'CAPLUS' ENTERED AT 10:17:20 ON 17 AUG 2005 USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT. PLEASE SEE "HELP USAGETERMS" FOR DETAILS. COPYRIGHT (C) 2005 AMERICAN CHEMICAL SOCIETY (ACS)

=> s (autoimmune disease or autoimmune encephalomyelit? or rheumatoid arthrit? or systemic lupus erythematos? or multiple sclerosis)

SINCE FILE

TOTAL

L2 136215 FILE MEDLINE L3 119817 FILE BIOSIS L4 136957 FILE EMBASE L5 60193 FILE CAPLUS

TOTAL FOR ALL FILES

L6 453182 (AUTOIMMUNE DISEASE OR AUTOIMMUNE ENCEPHALOMYELIT? OR RHEUMATOID
ARTHRIT? OR SYSTEMIC LUPUS ERYTHEMATOS? OR MULTIPLE SCLEROSIS)

=> s c20.111?

L7 0 FILE MEDLINE
L8 0 FILE BIOSIS
L9 0 FILE EMBASE

TERM '111?' EXCEEDED TRUNCATION LIMITS - SEARCH ENDED You have entered a truncated stem which occurs in too many terms. Make the stem longer and try again. For example, if your original term was 'degr?' to search for variations and the abbreviation for 'degradation', you could replace it with the expression '(degrdn OR degrad?)'. If your search term was numeric, e.g., 'C>5', reduce the size of the range.

=> s c20.111?/ct

L10 250623 FILE MEDLINE
L11 50150 FILE BIOSIS
L12 0 FILE EMBASE
L13 0 FILE CAPLUS

TOTAL FOR ALL FILES

L14 300773 C20.111?/CT

=> s l1 or "2,4-pyrimidinediamine" or "2,4-diaminopyridine" or nsc 30856 or r(w) (921302 or 926891 or 940323 or 940347 or 921303) or r921302 or r926891 or r940323 or r940347 or r921303

L15 39 FILE MEDLINE
L16 62 FILE BIOSIS
L17 35 FILE EMBASE
L18 351 FILE CAPLUS

```
Page 5
TOTAL FOR ALL FILES
           487 L1 OR "2,4-PYRIMIDINEDIAMINE" OR "2,4-DIAMINOPYRIDINE" OR NSC ·
L19
               30856 OR R(W) (921302 OR 926891 OR 940323 OR 940347 OR 921303)
               OR R921302 OR R926891 OR R940323 OR R940347 OR R921303
=> s 119 and (16 or 115)
            39 FILE MEDLINE
<---->User Break---->
SEARCH ENDED BY USER
=> s 119 and (16 or 114)
             O FILE MEDLINE
L22
             O FILE BIOSIS
L23
            1 FILE EMBASE
L24
L25
            12 FILE CAPLUS
TOTAL FOR ALL FILES
           13 L19 AND (L6 OR L14)
L26
=> dup rem 126
PROCESSING COMPLETED FOR L26
             13 DUP REM L26 (0 DUPLICATES REMOVED)
L27
=> d 1-13 ibib abs hitstr
L27 ANSWER 1 OF 13 CAPLUS COPYRIGHT 2005 ACS on STN
```

ACCESSION NUMBER:

2005:158647 CAPLUS

DOCUMENT NUMBER:

142:261547

TITLE:

Preparation of 2,4-

pyrimidinediamines useful in the treatment of

neoplastic diseases, inflammatory and immune system

disorders

INVENTOR (S):

Garcia-echeverria, Carlos; Kanazawa, Takanori; Kawahara, Eiji; Masuya, Keiichi; Matsuura, Naoko; Miyake, Takahiro; Ohmori, Osamu; Umemura, Ichiro; Steensma, Ruo; Chopiuk, Greg; Jiang, Jiqing; Wan, Yongqin; Ding, Qiang; Zhang, Qiong; Gray, Nathanael Schiander; Karanewsky, Donald

PATENT ASSIGNEE(S):

Novartis A.-G., Switz.; Novartis Pharma G.m.b.H.; IRM

LLC

2

SOURCE:

LANGUAGE:

PCT Int. Appl., 285 pp.

CODEN: PIXXD2

DOCUMENT TYPE:

Patent English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005016894	A1	20050224	WO 2004-EP9099	20040813
W: AE, AG,	AL, AM, AT,	AU, AZ,	BA, BB, BG, BR, BW	, BY, BZ, CA, CH,
CN, CO,	CR, CU, CZ,	DE, DK,	DM, DZ, EC, EE, EG	, ES, FI, GB, GD,
GE, GH,	GM, HR, HU,	ID, IL,	IN, IS, JP, KE, KG	, KP, KR, KZ, LC,
LK, LR,	LS, LT, LU,	LV, MA,	MD, MG, MK, MN, MW	, MX, MZ, NA, NI,
NO, NZ,	OM, PG, PH,	PL, PT,	RO, RU, SC, SD, SE	, SG, SK, SL, SY,
TJ, TM,	TN, TR, TT,	TZ, UA,	UG, US, UZ, VC, VN	, YU, ZA, ZM, ZW
RW: BW, GH,	GM, KE, LS,	MW, MZ,	NA, SD, SL, SZ, TZ	, UG, ZM, ZW, AM,
AZ, BY,	KG, KZ, MD,	RU, TJ,	TM, AT, BE, BG, CH	, CY, CZ, DE, DK,
EE, ES,	FI, FR, GB,	GR, HU,	IE, IT, LU, MC, NL	, PL, PT, RO, SE,

SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE,

SN, TD, TG

PRIORITY APPLN. INFO.: GB 2003-19227 A 20030815

GB 2003-22370 A 20030924

OTHER SOURCE(S): MARPAT 142:261547

GΙ

AB The title compds. I [R = aryl, heteroaryl, cycloalkyl and heterocycloalkyl; R0-R3 = H, alkyl, cycloalkyl, etc.; R4 = H, alkyl; R5, R6 = H, alkyl, alkoxyalkyl, etc.], useful for the manufacture of a medicament for the treatment or prevention of a disease which responds to inhibition of FAK and/or ALK and/or ZAP-70 and/or IGF-IR, were prepared and formulated. E.g., a 2-step synthesis of II, starting from 2,4-dichloro-5-nitropyrimidine and 2-amino-N-methylbenzenesulfonamide, was given. The compds. I have IC50 values in the range of 10 nM to 2 μ M in cell-free ZAP-70 kinase assay.

REFERENCE COUNT: 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L27 ANSWER 2 OF 13 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2005:158646 CAPLUS

DOCUMENT NUMBER: 142:254587

TITLE: Methods for treating or preventing autoimmune

diseases with 2,4-

pyrimidinediamine compounds

INVENTOR(S): Rajinder, Singh; Ankush, Argade; Li, Hui; Bhamidipati,

Somasekhar; Carroll, David; Sylvain, Catherine;

Clough, Jeffrey; Keim, Holger

PATENT ASSIGNEE(S): Rigel Pharmaceuticals, Inc., USA

SOURCE: PCT Int. Appl., 276 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 3

PATENT INFORMATION:

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DATE
                                              APPLICATION NO.
                                                                       DATE
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                                                                       _____
                                               WO 2004-US24716
                           A2
                                  20050224
     WO 2005016893
                                                                       20040730
     WO 2005016893
                           A3
                                  20050609
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              CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
             GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,
             LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI,
             NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY,
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             AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE,
              SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE,
              SN, TD, TG
PRIORITY APPLN. INFO.:
                                               US 2003-491641P
                                                                    P 20030730
                                                                    P
                                               US 2003-531598P
                                                                       20031219
                                                                    P 20040518
                                               US 2004-572246P
OTHER SOURCE(S):
                          MARPAT 142:254587
     The invention provides methods for treating or preventing
     autoimmune diseases with 2,4-
     pyrimidinediamine compds., as well as methods of treating,
     preventing or ameliorating symptoms associated with such diseases.
     examples of autoimmune diseases that can be treated or
     prevented with the compds. include rheumatoid arthritis
     and/or its associated symptoms, systemic lupus
     erythematosis and/or its associated symptoms and multiple .
     sclerosis and/or its associated symptoms.
     156-81-0D, 2,4-Pyrimidinediamine,
IT
     derivs.
     RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
     (Biological study); USES (Uses)
        (pyrimidinediamine compds. for treatment or prevention of
        autoimmune diseases)
RΝ
     156-81-0 CAPLUS
     2,4-Pyrimidinediamine (9CI) (CA INDEX NAME)
CN
```

```
L27 ANSWER 3 OF 13 CAPLUS COPYRIGHT 2005 ACS on STN
```

ACCESSION NUMBER: 2005:120923 CAPLUS

DOCUMENT NUMBER:

142:219300

TITLE:

2,4-Pyrimidinediamines

for use in the treatment or prevention of

autoimmune diseases

INVENTOR(S): Rajinder, Singh; Ankush,

Rajinder, Singh; Ankush, Argade; Li, Hui; Bhamidipati,

Somasekhar; Carroll, David; Sylvain, Catherine;

Clough, Jeffrey; Keim, Holger

PATENT ASSIGNEE(S):

Rigel Pharmaceuticals, Inc., USA

SOURCE:

PCT Int. Appl., 169 pp.

CODEN: PIXXD2

DOCUMENT TYPE:

Patent

Page 8

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 3

PATENT INFORMATION:

	PATENT NO.)	DATE		i	APPL:	ICAT:	ION I	NO.		D	ATE	
	WO 2	2005	0122	94		A1	-	2005	0210	1	WO 2	004-1	JS24:	920		2	0040	730
		W:	ΑE,	AG,	AL,	AM,	AT,	AU,	ΑZ,	BA,	BB,	BG,	BR,	B₩,	BY,	BZ,	CA,	CH,
			CN,	CO,	CR,	CU,	CZ,	DE,	DK,	DM,	DZ,	EC,	EE,	EG,	ES,	FI,	GB,	GD,
			GE,	GH,	GM,	HR,	HU,	ID,	IL,	IN,	IS,	JP,	ΚE,	KG,	KP,	KR,	KZ,	LC,
			LK,	LR,	LS,	LT,	LU,	LV,	MA,	MD,	MG,	MK,	MN,	MW,	MX,	MZ,	NA,	NI,
			NO,	NZ,	OM,	PG,	PH,	PL,	PT,	RO,	RU,	SC,	SD,	SE,	SG,	SK,	SL,	SY,
			ΤJ,	TM,	TN,	TR,	TT,	TZ,	UA,	UG,	US,	UZ,	VC,	VN,	YU,	ZA,	ZM,	ZW
		RW:	BW,	GH,	GM,	KE,	LS,	MW,	MZ,	NA,	SD,	SL,	SZ,	TZ,	UG,	ZM,	ZW,	AM,
			ΑZ,	BY,	KG,	ΚZ,	MD,	RU,	ТJ,	TM,	AT,	BE,	BG,	CH,	CY,	CZ,	DE,	DK,
			EE,	ES,	FI,	FR,	GB,	GR,	HU,	ΙE,	IT,	LU,	MC,	NL,	PL,	PT,	RO,	SE,
			SI,	SK,	TR,	BF,	ВJ,	CF,	CG,	CI,	CM,	GA,	GN,	GQ,	GW,	ML,	MR,	ΝE,
			SN,	TD,	TG													
PRIOR	YTI	APP	LN.	INFO	. :					1	US 2	003-4	4916	41P	:	P 2	0030	730
										1	US 2	003-	5315	98P	:	P 2	0031	219
										1	US 2	004-	5722	46P		P 2	0040	518
			/ - \															

OTHER SOURCE(S): MARPAT 142:219300

GI

The present invention provides methods of treating or preventing AΒ autoimmune diseases with 2,4pyrimidinediamine compds. I [L1, L2 = a direct bond or a linker; R2 = II; R4 = III; X = N, CH; Y, Z = O, S, SO, SO2, etc.; R5 = R6, alkyl,alkenyl, etc.; R6 = H, an electroneg. group, alkoxy, haloalkoxy, etc.; R31 = Me, alkyl; R35 = H, alkyl, cycloalkyl, etc.; or two R35 bonded together to the same carbon atom are taken together to form an oxo, (un)substituted NH], as well as methods of treating, preventing or ameliorating symptoms associated with such diseases. Specific examples of autoimmune diseases that can be treated or prevented with the compds. I include rheumatoid arthritis and/or its associated symptoms, systemic lupus erythematosus and/or its associated symptoms and multiple sclerosis and/or its associated symptoms. The general procedures for synthesis of compds. I are described. The characterization data for over 500 prepared

compds. I were given in table. The compds. I were tested in various tests (e.g., inhibition of IgE-induced degranulation, inhibition of Syk kinase, etc.). For example, N4-(2,2-dimethyl-3-oxo-4H-5-pyrido[1,4]oxazin-6-yl)-5fluoro-N2-(3,4,5-trimethoxyphenyl)-2,4-

pyrimidinediamine showed 99.8% inhibition of edema formation when administered at 5 mg/kg in mice.

REFERENCE COUNT: THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS 3 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L27 ANSWER 4 OF 13 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2004:220155 CAPLUS

DOCUMENT NUMBER: 140:270866

TITLE: Preparation of (pyridinyl) (pyrimidinyl) imidazo[1,2-

alpyridines as TGFB receptor type I antagonists for treatment of fibrotic disorders and tumors

Lee, Wen-cherng; Carter, Mary Beth; Sun, Lihong; Chuaqui, Claudio; Singh, Juswinder; Boriack-Sjodin, INVENTOR (S):

Paula; Choi, Michael S.

PATENT ASSIGNEE(S):

Biogen, Inc., USA PCT Int. Appl., 142 pp. SOURCE:

CODEN: PIXXD2

DOCUMENT TYPE: Patent English LANGUAGE:

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PA	TENT	NO.			KIN	D	DATE			APPL	ICAT:	IÓN 1	NO.		D	ATE	
	2004						2004		1	WO 2	003-1	US27	721		2	0030	905
WU	2004						2004										
	W:						ΑU,										
		CO,	CR,	CU,	CZ,	DΕ,	DK,	DM,	DΖ,	EC,	EE,	ES,	FI,	GB,	GD,	GE,	GH,
		GM,	HR,	HU,	ID,	IL,	IN,	IS,	JP,	KE,	KG,	KP,	KR,	KZ,	LC,	LK,	LR,
							MD,										
		-	-	-	-	-	RU,	•	•		•	•	•	•	•	•	•
							US,					-	-	-		•	•
	RW:	GH,					-	-	-	•			•		AM,	AZ,	BY,
							TM,										
							ΙE,										
							CM,										
, CA	2497	968			AA		2004	0318		CA 2	003-2	2497	968		20	0030	905
EP	1546	112			A2		2005	0629	1	EP 2	003-	7520	04		20	0030	905
		AT,															
							RO,										
BR	2003																905
PRIORIT											002-4						
			•								003-1					0030	
												,		•			

OTHER SOURCE(S): MARPAT 140:270866

GΙ

Title compds. I [wherein X1, X2, X3, X4 = independently CRx or N, only two AB of them can be N simultaneously; Y1, Y2 = independently CRa or N, at least one of them must be N; R1 = independently alkyl, alkenyl, alkynyl, alkoxy, acyl, urea, cycloalkylsulfanyl, etc.; R2 = independently alkyl, alkenyl, alkynyl, acyl, halo, -N(alkyl) (cycloalkyl), heteroaroyl, etc.; m = 0-4; n = 0-3; Rx, Ra = independently hydrogen, alkyl, alkenyl, hydroxy, guanidino, amidino, cycloalkylcarbonylamino, etc.; and pharmaceutically acceptable salts or N-oxides thereof] were prepared as antagonists against transforming growth factor β (TGF β) family type I receptors, Alk5 and Alk4. For example, methylation of 2-mercapto-4-methylpyrimidine with MeI, followed by reaction with 6-methylpyridine-2-carboxylic acid Et ester and cyclocondensation with 2-aminopyridine, gave II. I exhibited TGFβ-induced PAI-Luciferase reporter activity with IC50 values of less than $10\mu M$ and cytotoxicity with LD25 values greater than $10\mu M$. Thus, I and their pharmaceutical compns. are useful as antagonists for preventing and/or treating numerous diseases, including fibrotic disorders and tumors.

IT 156-81-0, 2,4-Diaminopyrimidine

RL: RCT (Reactant); RACT (Reactant or reagent) (preparation of (pyridinyl) (pyrimidinyl) imidazo[1,2-a] pyridines as TGF β receptor type I antagonists for treatment of fibrotic disorders and tumors)

RN 156-81-0 CAPLUS

CN 2,4-Pyrimidinediamine (9CI) (CA INDEX NAME)

L27 ANSWER 5 OF 13 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2004:142963 CAPLUS

DOCUMENT NUMBER: 140:199334

TITLE: Preparation of 2,4-pyrimidinediamines as IgE and/or

IgG receptor modulators for treatment of autoimmune

diseases

INVENTOR(S): Singh, Rajinder; Argade, Ankush; Payan, Donald G.;

Clough, Jeffrey; Keim, Holger; Sylvain, Catherine; Li,

Hui; Bhamidipati, Somasekhar

PATENT ASSIGNEE(S): Rigel Pharmaceuticals, USA

SOURCE: PCT Int. Appl., 811 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: English

Page 11

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PA'	PATENT NO.														I	DATE	
WO	2004	0143	82		A1		2004				2003-				2	20030	729
	W :	ΑE,	AG,	AL,	AM,	AT,	AU,	ΑZ,	BA,	BB	BG,	BR,	BY,	BZ,	CA,	CH,	CN,
		CO,	CR,	CU,	CZ,	DE,	DK,	DM,	DZ,	EC	E, EE,	ES,	FI,	GB,	GD,	GE,	GH,
		GM,	HR,	HU,	ID,	ΙL,	IN,	IS,	JP,	KE	KG,	ΚP,	KR,	KZ,	LC,	LK,	LR,
		LS,	LT,	LU,	LV,	MA,	MD,	MG,	MK,	MN	I, MW,	MX,	MZ,	NI,	NO,	NZ,	OM,
		PG,	PH,	PL,	PT,	RO,	RU,	SC,	SD,	SE	, SG,	SK,	SL,	SY,	ΤJ,	TM,	TN,
		TR,	TT,	TZ,	UΑ,	UG,	US,	UΖ,	VC,	VN	I, YU,	ZA,	ZM,	ZW			
	RW:	GH,	GM,	KE,	LS,	MW,	MZ,	SD,	SL,	SZ	, TZ,	UG,	ZM,	ZW,	AM,	AZ,	BY,
		KG,	KZ,	MD,	RU,	TJ,	TM,	AT,	BE,	BG	, CH,	CY,	CZ,	DE,	DK,	EE,	ES,
		FI,	FR,	GB,	GR,	HU,	ΙE,	IT,	LU,	MC	NL,	PT,	RO,	SE,	SI,	SK,	TR,
		BF,	ВJ,	CF,	CG,	CI,	CM,	GA,	GN,	GÇ	, GW,	ML,	MR,	ΝE,	SN,	TD,	TG
CA	2492	325			AA		2004	0219	(CA	2003-	2492	325		2	0030	729
EP	1534	286			A1		2005	0601	I	ΞP	2003-	7848	71		2	0030	729
	R:	AT,	BE,	CH,	DE,	DK,	ES,	FR,	GB,	GR	, IT,	LI,	LU,	NL,	SE,	MC,	PT,
		ΙE,	SI,	LT,	LV,	FI,	RO,	MK,	CY,	ΑL	TR,	BG,	CZ,	EE,	HU,	SK	
											2003-						
											2004-					0040	601
							2005	0329	5	SE	2005-	203			2	0050	
PRIORIT	Y APP	LN. :	INFO	. :							2002-					0020	72·9
				•							2003-		_			0030	131
									τ	JS	2003-	4523	39P		P 2	0030	306
											2003-					0030	729
									Ţ	JS	2002-	3532	67P		P 2	0020	201
											2002-					0020	201
											2002-					0021	
											2003-						
											2003-1					0030	729
OTHER S	TIRCE	(s):			MARI	РΔТ	140 -	1993	34								

OTHER SOURCE(S): GI

MARPAT 140:199334

AΒ The present invention provides methods of treating or preventing autoimmune diseases with 2,4-pyrimidinediamine compds., as well as methods of treating, preventing or ameliorating symptoms associated with such diseases. Title compds. I [wherein L1 and L2 = independently a bond or a

linker; R2 = (un)substituted alkyl, (hetero)cycloalkyl, or (hetero)aryl; R4 = H or R2; R5 = R6 or (un) substituted alkyl, alkenyl, or alkynyl; R6 = independently H, an electroneg. group, protected alc. or thiol, haloalkyl(oxy), halo, CN, NC, OCN, SCN, NO, NO2, N3, or (un)substituted amino, sulfamoyl(oxy), acyl, carboxy, carbamoyl, (hetero)aryl(alkyl), etc.; with provisos and exclusions; and salts, hydrates, solvates, N-oxides, and prodrugs thereof] were prepared as inhibitors of the IgE and/or IqG receptor signaling cascades that lead to the release of chemical mediators. For example, coupling of 2,4-dichloropyrimidine with 4-ethoxyaniline in EtOH provided N2, N4-bis(4-ethoxyphenyl)-2,4pyrimidinediamine (II). The latter inhibited degranulation of bone marrow derived mast cells challenged with anti-IgE and ionomycin with IC50 values of 4.5 μM and 4.4 μM , resp. Thus, I and their pharmaceutical compns. are useful in the treatment and prevention of diseases characterized by, caused by, or associated with the release of chemical mediators via degranulation of mast, basophil, neutrophil, or eosinophil cells and other processes effected by activation of the IgE and/or IgG receptor signaling cascades. Specific examples of autoimmune diseases that can be treated or prevented with I and their pharmaceutical compns. include rheumatoid arthritis, systemic lupus erythematosis, and multiple sclerosis (no data).

REFERENCE COUNT: 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L27 ANSWER 6 OF 13 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2004:20322 CAPLUS

DOCUMENT NUMBER: 140:87658

TITLE: Peptidomimetic modulators of cell adhesion

INVENTOR(S): Gour, Barbara J.; Blaschuk, Orest W.; Ali, Anmar; Ni,

Feng; Chen, Zhigang; Michaud, Stephanie Denise; Wang,

Shaomeng; Hu, Zengjian

PATENT ASSIGNEE(S): Can.

SOURCE: U.S. Pat. Appl. Publ., 280 pp., Cont.-in-part of U.S.

Ser. No. 6,982.

CODEN: USXXCO

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 15

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004006011	A1	20040108	US 2003-425557	20030428
US 6031072	Α	20000229	US 1997-893534	19970711
US 6326352	B1	20011204	US 2000-507102	20000217
US 2002168761	A1	20021114	US 2001-769145	20010124
US 2002151475	A1	20021017	US 2001-6982	20011204
US 6914044	B2	20050705		
PRIORITY APPLN. INFO.:			US 1996-21612P	19960712
			US 1997-893534	A1 19970711
			US 2000-491078	32 20000124
			US 2000-507102	1 20000217
			US 2001-769145	32 20010124
			US 2001-6982	A2 20011204

OTHER SOURCE(S): MARPAT 140:87658

AB Peptidomimetics of cyclic peptides, and compns. comprising such peptidomimetics are provided. The peptidomimetics have a three-dimensional structure that is substantially similar to a three-dimensional structure of a cyclic peptide that comprises a cadherin cell adhesion recognition sequence HAV. Methods for using such

peptidomimetics for modulating cadherin-mediated cell adhesion in a variety of contexts are also provided.

L27 ANSWER 7 OF 13 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER:

2003:737756 CAPLUS

DOCUMENT NUMBER:

139:261319

TITLE:

Preparation of 5-bromo-2,4-

pyrimidinediamines and related compounds as

cyclin dependent kinase inhibitors

INVENTOR (S):

Luecking, Ulrich; Krueger, Martin; Jautelat, Rolf;

Prien, Olaf; Siemeister, Gerd; Ernst, Alexander

PATENT ASSIGNEE(S):

Schering Aktiengesellschaft, Germany

SOURCE:

PCT Int. Appl., 116 pp.

CODEN: PIXXD2

DOCUMENT TYPE:

Patent German

LANGUAGE:

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

I	PAT	ENT I	NO.			KIN	D	DATE			APPL	ICAT	ION I	NO.		D	ATE	
V	10	2003	0764	37		A1	_	2003	0918	,	WO 2	003-	EP19	95		2	0030	226
		W:	ΑE,	AG,	AL,	AM,	AT,	AU,	AZ,	BA,	BB,	BG,	BR,	BY,	ΒZ,	CA,	CH,	CN,
			CO,	CR,	CU,	CZ,	DK,	DM,	DZ,	EC,	EE,	ES,	FI,	GB,	GD,	GE,	GH,	GM,
			HR,	HU,	ID,	IL,	IN,	IS,	JP,	ΚE,	KG,	ΚP,	KR,	ΚZ,	LC,	LK,	LR,	LS,
			LT,	LU,	LV,	MA,	MD,	MG,	MK,	MN,	MW,	MX,	MZ,	NO,	NZ,	OM,	PH,	PL,
			PT,	RO,	RU,	SC,	SD,	SE,	SG,	SK,	SL,	ТJ,	TM,	TN,	TR,	TT,	TZ,	UA,
			UG,	UZ,	VC,	VN,	YU,	ZA,	ZM,	ZW								
		RW:	GH,	GM,	ΚE,	LS,	MW,	MZ,	SD,	SL,	SZ,	TZ,	UG,	ZM,	ZW,	AM,	ΑZ,	BY,
			KG,	ΚZ,	MD,	RU,	TJ,	TM,	AT,	ΒE,	BG,	CH,	CY,	CZ,	DE,	DK,	EE,	ES,
			FI,	FR,	GB,	GR,	HU,	ΙE,	IT,	LU,	MC,	NL,	PT,	SE,	SI,	SK,	TR,	BF,
			ВJ,	CF,	CG,	CI,	CM,	GA,	GN,	GQ,	GW,	ML,	MR,	ΝE,	SN,	TD,	TG	
Ĺ	ÞΕ	10212	2100			A1		2003	1023	1	DE 2	002-	1021	2100		2	0020	311
Ε	ÞΕ	1025	5984			A1		2004	0812]	DE 2	002-	1025	5984		2	0021	126
E	ΞP	14832	260			A1		2004	1208		EP 2	003-	7081	51		2	0030	226
		R:	AT,	ΒE,	CH,	DE,	DK,	ES,	FR,	GB,	GR,	IT,	LI,	LU,	NL,	SE,	MC,	PT,
			ΙE,	SI,	LT,	LV,	FI,	RO,	MK,	CY,	AL,	TR,	BG,	CZ,	EE,	HU,	SK	
τ	JS	20040	0637	37		A 1		2004	0401	1	US 2	003-3	3847	87		2	0031	027
PRIORI	ΙΤΥ	APPI	LN.	INFO	. :							002-3				A 2	0020	311
												002-			-	A 2	0021	126
										1	US 2	002-3	3638	78P]	P 2	0020	314
												002-4				-	0021	
											WO 2	003-1	EP19:	95	Ī	₩ 2	0030	226
OTHER	ടവ	HRCE	(s) .			MAR	РΔТ	139.	2613:	19								

OTHER SOURCE(S):

MARPAT 139:261319

GΙ

Title compds. I and II [D, E, G, L, M, T = C, O, N, S atom whereby at least a heteroatom must be contained in the ring; R1 = H, halo, alkyl, etc.; R2 = H, alkyl, alkenyl, etc.; A, B = H, OH, halo, etc.; n = 0, 1 with provisos] and their pharmaceutically acceptable salts were prepared For example, condensation of chloropyrimidine III, e.g., prepared from 5-bromo-2-chloro-4-hydroxypyrimidine in 2-steps, and threo-3-methylaminobutan-2-ol afforded pyrimidinediamine IV in 75% yield. In CDK2/CycE inhibition studies, 24-examples of compds. I exhibited IC50 values ranging from 6-74 nM. Compds. I are claimed useful as cardiovascular, antiviral, antitumor, etc. agents.

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L27 ANSWER 8 OF 13 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2003:133036 CAPLUS

DOCUMENT NUMBER: 138:180679

TITLE: SH3 protein domains and their ligands

INVENTOR(S): Booker, Grant William; Pyke, Simon Mathew; Branson,

Kim Mathew; Inglis, Steven Robert

PATENT ASSIGNEE(S): Adelaide Research & Innovation Pty Ltd., Australia

SOURCE: PCT Int. Appl., 176 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND DATE	APPLICATION NO.	DATE
WO 2003013523	A1 20030220	WO 2002-AU1064	20020808
W: AE, AG, AL,	AM, AT, AU, AZ,	BA, BB, BG, BR, BY, BZ,	CA, CH, CN,
CO, CR, CU,	CZ, DE, DK, DM,	DZ, EC, EE, ES, FI, GB,	GD, GE, GH,
GM, HR, HU,	ID, IL, IN, IS,	JP, KE, KG, KP, KR, KZ,	LC, LK, LR,

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LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,
             PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ,
             UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD,
             RU, TJ, TM
         RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG,
             CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL,
             PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR,
             NE, SN, TD, TG
                                            AU 2001-6881
                                                                A 20010808
PRIORITY APPLN. INFO.:
                         MARPAT 138:180679
OTHER SOURCE(S):
    The present invention relates generally to mols. capable of interaction
     with one or more domains within a proteinaceous mol. such as a peptide,
     polypeptide, protein or a macromol. comprising a proteinaceous mol. More
     particularly the present invention relates to mols. including ligands
     which are capable of interacting with, and more particularly, binding to,
     SH3 protein domains or homologs thereof and even more particularly to
     mols. including ligands which are capable of binding to SH3 domains having
     a three-dimensional ligand-binding site comprising a neg. charged residue
     and a hydrophobic residue linearly separated by at least five amino acid
     residues. The subject invention is preferably directed to the use of
     2-aminopyridine, 2-aminoquinoline, 1-aminoisoquinoline and derivs.,
     homologs, analogs and mimetics thereof or pharmaceutically acceptable
     salts thereof which interact with SH3 domains, and more particularly to
     the binding of 2-aminopyridine, 2-aminoquinoline, 1-aminoisoquinoline and
     derivs. analogs and mimetics to SH3 domains as defined above. The present
     invention contemplates the use of a three dimensional structure of the
     subject SH3 domain to identify, screen and design amino-substituted and
     amino-substituted pyridines and aminoquinolines capable of binding to an
     SH3 domain. The present invention is also useful for the in silico
     selection of derivs. homologs, analogs and mimetics of 2-aminopyridine,
     2-aminoquinoline, 1-aminoisoquinoline capable of binding to SH3 domains.
     The ligands of the present invention are useful in the development of a
     range of therapeutic and diagnostic agents.
                               THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS
REFERENCE COUNT:
                               RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT
L27 ANSWER 9 OF 13 CAPLUS COPYRIGHT 2005 ACS on STN
                         2003:91269 CAPLUS
ACCESSION NUMBER:
                         139:62596
DOCUMENT NUMBER:
                         Imidazopyrimidines, potent inhibitors of p38 MAP
TITLE:
                         kinase
                         Rupert, Kenneth C.; Henry, James R.; Dodd, John H.;
AUTHOR(S):
                         Wadsworth, Scott A.; Cavender, Druie E.; Olini,
                         Gilbert C.; Fahmy, Bohumila; Siekierka, John J.
                         L.L.C., Drug Discovery, Johnson & Johnson
CORPORATE SOURCE:
                         Pharmaceutical Research and Development, Raritan, NJ,
                         08869, USA
                         Bioorganic & Medicinal Chemistry Letters (2003),
SOURCE:
                         13(3), 347-350
                         CODEN: BMCLE8; ISSN: 0960-894X
                         Elsevier Science Ltd.
PUBLISHER:
DOCUMENT TYPE:
                         Journal
                         English
LANGUAGE:
                         CASREACT 139:62596
OTHER SOURCE(S):
     The MAP kinase p38 is implicated in the release of the pro-inflammatory
     cytokines TNF-\alpha and IL-1\beta. Inhibition of cytokine release may
     be a useful treatment for inflammatory conditions such as
     rheumatoid arthritis and Crohn's disease. A novel
     series of imidazopyrimidines have been discovered that potently inhibit
     p38 and suppress the production of TNF-\alpha in vivo.
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Page 16

156-81-0, 2,4-Pyrimidinediamine IT

RL: RCT (Reactant); RACT (Reactant or reagent)

(imidazopyrimidines, potent inhibitors of p38 MAP kinase)

RN156-81-0 CAPLUS

2,4-Pyrimidinediamine (9CI) (CA INDEX NAME) CN

NH₂ H₂N_\

REFERENCE COUNT: 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L27 ANSWER 10 OF 13 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2002:449449 CAPLUS

DOCUMENT NUMBER: 137:33318

Preparation of pyrimidinylaminothiazoles as tyrosine TITLE:

kinase inhibitors.

INVENTOR(S): Bilodeau, Mark T.; Hartman, George D.; Hoffman, Jacob

> M., Jr.; Lumma, William C., Jr.; Manley, Peter J.; Rodman, Leonard; Sisko, John T.; Smith, Anthony M.;

Tucker, Thomas J.

PATENT ASSIGNEE(S): Merck & Co., Inc., USA

SOURCE: PCT Int. Appl., 169 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent English LANGUAGE:

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PATENT NO.		KIN	D DATE	<u> </u>	AI	PPLI	CATI	ON 1	10.		D	ATE	
WO 2002045	652	A2	2002	20613	WC	20	01-U	IS445	573		20	0011	L30
WO 2002045	652	A3	2002	20822									
W: AE	, AG, 1	AL, AM,	AT, AU,	AZ,	BA, I	ВB,	BG,	BR,	BY,	ΒZ,	CA,	CH,	CN,
CC	, CR,	CU, CZ,	DE, DK,	DM,	DZ, E	ΞC,	EE,	ES,	FI,	GB,	GD,	GE,	GH,
GM	, HR, 1	HU, ID,	IL, IN,	IS,	JP, H	ΚE,	KG,	KR,	ΚZ,	LC,	LK,	LR,	LS,
LT	', LU, :	LV, MA,	MD, MG,	MK,	MN, N	νW,	MX,	MZ,	NO,	NZ,	OM,	PH,	PL,
PT	, RO, 1	RU, SD,	SE, SG,	SI,	SK, S	SL,	TJ,	TM,	TR,	TT,	TZ,	UA,	UG,
US	, UZ,	VN, YU,	ZA, ZM,	ZW,	AM, A	ΑZ,	BY,	KG,	KΖ,	MD,	RU,	TJ,	TM
RW: GH	, GM, :	KE, LS,	MW, MZ,	SD,	SL, S	SZ,	ΤZ,	UG,	ZM,	ZW,	AT,	BE,	CH,
CA	, DE, 1	DK, ES,	FI, FR,	GB,	GR,	ΙE,	IT,	LU,	MC,	NL,	PT,	SE,	TR,
BF	, BJ, (CF, CG,	CI, CM,	GA,	GN, C	GQ,	GW,	ML,	MR,	ΝE,	SN,	TD,	TG
US 2002137	755	A1	2002	20926	บร	5 20	01-9	9047	73		20	0011	121
CA 2429728		AA	2002	20613	C	A 20	01-2	4297	728		20	0011	130
AU 2002032	441	A5	2002	20618	Α	J 20	02-3	2441	L		20	0011	L30
EP 1341540		A2	2003	30910	EI	P 20	01-9	9196	55		20	0011	L30
R: AT	, BE, (CH, DE,	DK, ES,	FR,	GB, C	GR,	IT,	LI,	LU,	NL,	SE,	MC,	PT,
IE	, SI,	LT, LV,	FI, RO,	MK,	CY, A	AL,	TR						
JP 2004524	282	T2	2004	10812	JI	P 20	02-5	4743	8 8		20	0011	L30
US 2004063	720	A1	2004	0401	US	3 20	03-6	7768	37		20	0031	002
PRIORITY APPLN.	INFO.	:			US	S 20	00-2	5100)6P	I	2 (00012	204
					US	3 20	01-9	9047	73	1	A1 20	011:	L21
					WC	20	01-U	IS445	573	V	1 20	011:	L30
OTHER SOURCE(S)	:	MAR	PAT 137:	33318	3								

OTHER SOURCE(S):

GΙ

Title compds. [I; A, B = N, NO; Y = O, S, NR4; R1, R2 = H, perfluoroalkoxy, OH, cyano, halo, (substituted) alkyl(oxy)(carbonyl), aryl(oxy)(carbonyl), heterocyclyl, etc.; R4 = H, aryl, alkyl; R5 = H,
SO2Rc, CORc, Rc, CO2Rc; R6 = aryl, cyano, halo, (substituted) alkyl, alkenyl, alkynyl, heterocyclyl, aminocarbonyl; Rc = alkyl, aryl, heterocyclyl], were prepared for treating angiogenesis, cancer, tumor growth, atherosclerosis, age related macular degeneration, diabetic retinopathy, inflammation, etc. Thus, 4-aminopyrimidine was stirred with NaH in THF; 2-bromo-5-phenylthiazole was added and the mixture was refluxed overnight to give 5-phenylthiazol-2-yl pyrimidin-4-yl amine. I inhibited vascular endothelial growth factor-stimulated mitogenesis of human vascular endothelial cells with IC50 = 0.01-5.0 nM.

156-81-0, 2,4-Diaminopyrimidine

RL: RCT (Reactant); RACT (Reactant or reagent) (preparation of pyrimidinylaminothiazoles as tyrosine kinase inhibitors)

RN156-81-0 CAPLUS

CN 2,4-Pyrimidinediamine (9CI) (CA INDEX NAME)

CAPLUS COPYRIGHT 2005 ACS on STN L27 ANSWER 11 OF 13

ACCESSION NUMBER:

2002:869496 CAPLUS

DOCUMENT NUMBER:

137:363033

TITLE:

Peptidomimetic modulators of cell adhesion

INVENTOR(S):

Gour, Barbara J.; Blaschuk, Orest W.; Ali, Anmar; Ni,

Feng; Chen, Zhigang; Michaud, Stephanie D.; Wang,

Shoameng; Hu, Zenjian

PATENT ASSIGNEE (S):

Can.

SOURCE:

U.S. Pat. Appl. Publ., 309 pp., Cont.-in-part of U.S.

Ser. No. 491,078.

CODEN: USXXCO

DOCUMENT TYPE:

Patent English

LANGUAGE:

15

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	_	DATE
US 2002168761	A1	20021114	US 2001-769145		20010124
US 2004058864	A1	20040325	US 2003-412701		20030410
US 2004006011	A1	20040108	US 2003-425557		20030428
PRIORITY APPLN. INFO.:			US 2000-491078	A2	20000124
			US 1996-21612P	P	19960712
			US 1997-893534	A1	19970711

US 2000-507102 A1 20000217 US 2001-769145 B1 20010124 US 2001-6982 A2 20011204

OTHER SOURCE(S): MARPAT 137:363033

AB Peptidomimetics of cyclic peptides, and compns. comprising such peptidomimetics are provided. The peptidomimetics have a three-dimensional structure that is substantially similar to a three-dimensional structure of a cyclic peptide that comprises a cadherin cell adhesion recognition sequence HAV. Methods for using such peptidomimetics for modulating cadherin-mediated cell adhesion in a variety of contexts are also provided.

L27 ANSWER 12 OF 13 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2000:457043 CAPLUS

DOCUMENT NUMBER:

133:89537

TITLE:

Preparation of 2,4-

pyrimidinediamine derivatives as anticancer

agents

INVENTOR (S):

Bradbury, Robert Hugh; Breault, Gloria Anne; Jewsbury,

Philip John; Pease, Janet Elizabeth

PATENT ASSIGNEE(S):

Astrazeneca UK Limited, UK

SOURCE:

PCT Int. Appl., 137 pp.

CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

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	2000															9991:	
	W:	ΑE,	AL,	AM,	AT,	AU,	ΑZ,	BA,	BB,	ВG,	BR,	BY,	CA,	CH,	CN,	CR,	CU,
		CZ,	DE,	DK,	DM,	EE,	ES,	FI,	GB,	GD,	GE,	GH,	GM,	HR,	HU,	ID,	IL,
		IN,	IS,	JP,	KE,	KG,	KP,	KR,	KZ,	LC,	LK,	LR,	LS,	LT,	LU,	LV,	MA,
		MD,	MG,	MK,	MN,	MW,	MX,	NO,	NZ,	PL,	PT,	RO,	RU,	SD,	SE,	SG,	SI,
		SK.	SL,	TJ,	TM,	TR,	TT,	TZ,	UA,	UG,	US,	UZ,	VN,	YU,	ZA,	ZW,	AM,
	-	-					RU,			·	•	•	•	•	•		
	RW:	GH,	GM,	KE,	LS,	MW,	SD,	SL,	SZ,	TZ,	UG,	ZW,	AT,	BE,	CH,	CY,	DE,
							GR,										
							GW,										
CA	2352	896	-	-	AA		2000	0706		CA 1	999-	2352	896		1	9991	220
	1140															9991	
EP	1140	860			В1		2004	0922									
	R:	ΑT,	BE,	CH,	DE,	DK,	ES,	FR,	GB,	GR,	IT,	LI,	LU,	NL,	SE,	MC,	PT,
		IE,	SI,	LT,	LV,	FI,	RO										
BR	9916	590			Α		2001	1023		BR 1	999-	1659	0		1	9991	220
JP	2002	5334	46		T 2		2002	1008		JP 2	000-	5910	12		1	9991:	220
AU	7630	91			В2		2003	0710		AU 2	000-	1874	3		1	9991	220
	5121						2003	0829		NZ 1	999-	5121	18		1	9991	220
AT	2770	20			E		2004	1015		AT 1	999-	9623	75		1	9991:	220
	2228						2005	0401		ES 1	999-	9623	75		1	9991	220
ZA	2001	0044	13		Α		2002	0829		ZA 2	001-	4413			2	0010	529
NO	2001	0030	38		Α		2001	0822]	NO 2	001-	3038			2	0010	619
	6593						2003	0715	1	US 2	001-	8686	02		2	0010	823
PRIORIT	Y APP	LN.	INFO	. :					(GB 1	998-	2851	1	7	A 1	9981	224
									1	WO 1	999-	GB43	25	1	W 1	9991:	220
	~****	(0)				- a m	122	0050	-								

OTHER SOURCE(S):

MARPAT 133:89537

GΙ

The present invention relates to the title compds. (I) [wherein R1 = H, AB (un) substituted alkyl, alkenyl, or alkynyl, benzyl, 2-phenylethyl, phthalimidoalkyl, or cycloalkylalkyl; Rx = halo, OH, NO2, NH2, CN, SH, CO2H, SO2NH2, NHCHO, ureido, etc.; Q1 and Q2 = independently (un) substituted aryl, 5- or 6-membered monocycle, or 9- or 10-membered bicyclic heterocycle], processes for their manufacture, and pharmaceutical compns. containing them. For example, addition of 4-[2-hydroxy-3-(N,Ndimethylamino)propoxy]aniline.HCl in MeOH to 5-bromo-2-chloro-4-(indan-5-ylamino)pyrimidine in BuOH (prepns. given) and heating to 100°C for 18 h gave II (42%). I inhibited the effects of cylin-dependent serine/threonine kinases (CDKs), showing selectivity for CDK2 (no data), CDK4 (IC50 ranging from 0.02 μM to 0.07 μM), and CDK6 (no data). a tyrosine kinase activity assay using Sf21 cells transfected with plaque-pure FAK recombinant virus, I also inhibited focal adhesion kinase 3 (FAK3) with IC50 ranging from 0.032 μ M to 0.07 μ M. Typical IC50 values for I when tested for inhibition of cell growth in an Sulforhodamine B (SRB) assay were in the range of 1 mM to 1 nM. possess anti-cancer properties, including anti-cell-migration, antiproliferation and/or apoptotic properties. Such properties are expected to be of value in the treatment of disease states associated with aberrant cell cycles and cell proliferation such as cancers (solid tumors and leukemias), fibroproliferative and differentiative disorders, psoriasis, rheumatoid arthritis, Kaposi's sarcoma, hemangioma, acute and chronic nephropathies, atheroma, atherosclerosis, arterial restenosis, autoimmune diseases, acute and chronic inflammation, bone diseases, and ocular diseases with retinal vessel proliferation.

REFERENCE COUNT: THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L27 ANSWER 13 OF 13 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED. on STN

ACCESSION NUMBER: 91081327 EMBASE

DOCUMENT NUMBER: 1991081327

Therapy of acute and chronic multiple TITLE:

sclerosis.

AUTHOR: Tindall R.S.A.

Department of Neurology, University of Southern California, CORPORATE SOURCE:

Los Angeles Veterans Administration Facility, 425 South

Hill Street, Los Angeles, CA 90013, United States

Comprehensive Therapy, (1991) Vol. 17, No. 1, pp. 18-25. SOURCE: ISSN: 0098-8243 CODEN: COTHD3

COUNTRY: United States

Journal; Article DOCUMENT TYPE:

Page 20

Neurology and Neurosurgery FILE SEGMENT: 800 Immunology, Serology and Transplantation 026 Drug Literature Index 037 LANGUAGE: English ENTRY DATE: Entered STN: 911216 Last Updated on STN: 911216 DATA NOT AVAILABLE FOR THIS ACCESSION NUMBER => s singh r?/au;s argade a?/au;s payan d?/au 2983 FILE MEDLINE 7931 FILE BIOSIS L29 2556 FILE EMBASE L30 9987 FILE CAPLUS L31 TOTAL FOR ALL FILES 23457 SINGH R?/AU L32 1 FILE MEDLINE L33 L34 8 FILE BIOSIS L35 7 FILE EMBASE L36 21 FILE CAPLUS TOTAL FOR ALL FILES 37 ARGADE A?/AU L37 144 FILE MEDLINE L38 L39 206 FILE BIOSIS L40138 FILE EMBASE L41 158 FILE CAPLUS TOTAL FOR ALL FILES 646 PAYAN D?/AU => s 132 and 137 and 142 O FILE MEDLINE L441 FILE BIOSIS L45 O FILE EMBASE L46 2 FILE CAPLUS TOTAL FOR ALL FILES 3 L32 AND L37 AND L42 => s 147 not 126 O FILE MEDLINE L49 1 FILE BIOSIS L50 O FILE EMBASE L51 1 FILE CAPLUS TOTAL FOR ALL FILES L52 2 L47 NOT L26 => dup rem 152 PROCESSING COMPLETED FOR L52 2 DUP REM L52 (0 DUPLICATES REMOVED) L53 => d ibib abs 1-2

L53 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2005 ACS on STN 2003:610204 CAPLUS

ACCESSION NUMBER:

DOCUMENT NUMBER: 139:164801

TITLE: Preparation of 2,4-pyrimidinediamines as IgE and/or

> IgG receptor modulators for treatment of allergic diseases, inflammatory conditions, and tissue

destruction

INVENTOR(S): Singh, Rajinder; Argade, Ankush;

Payan, Donald G.; Molineaux, Susan; Holland,

Sacha J.; Clough, Jeffrey; Keim, Holger; Bhamidipati, Somasekhar; Sylvain, Catherine; Li, Weigun; Rossi,

Alexander B.

PATENT ASSIGNEE (S): Rigel Pharmaceuticals, Inc., USA

SOURCE: PCT Int. Appl., 648 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

	PA'	CENT 1	NO.			KIN)	DATE			APPL	ICAT	ION :	NO.		D	ATE	
							-									-		
	WO	2003	0637	94		A2		2003	0807	1	WO 2	003-	US30	22		2	0030	131
	WO	2003	0637	94		A3		2003	1204									
		W:	ΑE,	AG,	AL,	AM,	ΑT,	AU,	AZ,	BA,	BB,	BG,	BR,	BY,	BZ,	CA,	CH,	CN,
								DK,										
								IN,										
								MD,										
								SD,										
								VN,					,	,		,	,	,
		RW:		•		•		MZ,	•	•	•		UG.	ZM.	ZW.	AM.	AZ.	BY.
								TM,										
								IE,										
			-	-				GA,							•	•	•	,
	CA	2474	-	-	•	ΑÁ	-	2003				•	•	•	•	•		131
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		1471				A2		2004										
		R:						ES,										
				-				RO,	-						•			,
	JP	2005						2005									0030	131
	US	2005	0382	43		A1											0040	
	US 2005038243 A1 PRIORITY APPLN. INFO.:											002-					0020	
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												003-1		_			0030	
			<i>(</i> ~ <i>)</i>									'						

OTHER SOURCE(S): MARPAT 139:164801

GI

Title compds. I [wherein L1 and L2 = independently a bond or a linker; R2 ΑB = (un) substituted alkyl, (hetero) cycloalkyl, or (hetero) aryl; R4 = H or R2; R5 = R6 or (un) substituted alkyl, alkenyl, or alkynyl; R6 = independently H, an electroneg. group, protected alc. or thiol, haloalkyl(oxy), halo, CN, NC, OCN, SCN, NO, NO2, N3, or (un) substituted amino, sulfamoyl(oxy), acyl, carboxy, carbamoyl, (hetero)aryl(alkyl), etc.; with provisos and exclusions; and salts, hydrates, solvates, N-oxides, and prodrugs thereof] were prepared as inhibitors of the IgE and/or IgG receptor signaling cascades that lead to the release of chemical mediators. For example, coupling of 2,4-dichloropyrimidine with 4-ethoxyaniline in EtOH provided N2,N4-bis(4-ethoxyphenyl)-2,4pyrimidinediamine (II). The latter inhibited degranulation of bone marrow derived mast cells challenged with anti-IgE and ionomycin with IC50 values of 4.5 μM and 4.4 $\mu M,$ resp. Thus, I and their pharmaceutical compns. are useful in the treatment and prevention of diseases characterized by, caused by, or associated with the release of chemical mediators via degranulation of mast, basophil, neutrophil, or eosinophil cells and other processes effected by activation of the IgE and/or IgG receptor signaling cascades. The treatment and prevention of allergic diseases, low grade scarring, diseases associated with tissue destruction, diseases associated with tissue inflammation, inflammation, and scarring are targeted uses (no data).

ΙI

L53 ANSWER 2 OF 2 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN

2002:165568 BIOSIS ACCESSION NUMBER: DOCUMENT NUMBER: PREV200200165568

Development and utilization of cultured human mast cells TITLE:

for high throughput small molecule drug discovery.

Rossi, Alexander [Reprint author]; Holland, Sacha [Reprint AUTHOR (S):

author]; Woronicz, John [Reprint author]; Quast, Jeff

[Reprint author]; Argade, Ankush; Sylvain,

Catherine; Juencke, Sara; Sula, Caroline; Tombo, Wendy

[Reprint author]; Goodrich, Bethany; Pine, Polly;

Scheerens, Heleen; Natarajan, Gita; Li, Wenbao; Bennett, Mark [Reprint author]; Daniel, Ruby; Wagner, Gregory; Singh, Rajinder; Molineaux, Susan [Reprint author];

Payan, Donald

Cell Biology, Rigel Pharmaceuticals, Inc., 240 East Grand CORPORATE SOURCE:

Avenue, So. San Francisco, CA, 94080, USA

Molecular Biology of the Cell, (Nov, 2001) Vol. 12, No. SOURCE:

Supplement, pp. 512a-513a. print.

Meeting Info.: 41st Annual Meeting of the American Society

```
for Cell Biology. Washington DC, USA. December 08-12, 2001.
                    American Society for Cell Biology.
                    CODEN: MBCEEV. ISSN: 1059-1524.
DOCUMENT TYPE:
                    Conference; (Meeting)
                    Conference; Abstract; (Meeting Abstract)
LANGUAGE:
                    English
ENTRY DATE:
                    Entered STN: 5 Mar 2002
                    Last Updated on STN: 5 Mar 2002
=> s keim h?/au;s bhamidipati s?/au;s sylvain c?/au;s li h?/au
L54
            84 FILE MEDLINE
L55
            57 FILE BIOSIS
L56
            57 FILE EMBASE
L57
           70 FILE CAPLUS
TOTAL FOR ALL FILES
           268 KEIM H?/AU
             8 FILE MEDLINE
            18 FILE BIOSIS
L60
L61
            7 FILE EMBASE
            16 FILE CAPLUS
TOTAL FOR ALL FILES
L63
           49 BHAMIDIPATI S?/AU
            8 FILE MEDLINE
L64
L65
            13 FILE BIOSIS
L66
            11 FILE EMBASE
L67
            10 FILE CAPLUS
TOTAL FOR ALL FILES
L68
          42 SYLVAIN C?/AU
L69
          5342 FILE MEDLINE
L70
          6316 FILE BIOSIS
L71
         4069 FILE EMBASE
L72
         21181 FILE CAPLUS
TOTAL FOR ALL FILES
         36908 LI H?/AU
=> s 158 and 163 and 168 and 173
L74
             0 FILE MEDLINE
L75
             0 FILE BIOSIS
L76
             0 FILE EMBASE
L77
             3 FILE CAPLUS
TOTAL FOR ALL FILES
L78
             3 L58 AND L63 AND L68 AND L73
=> s 178 not 152
L79
             0 FILE MEDLINE
L80
             0 FILE BIOSIS
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Prepared by: Mary Hale @2-2507 Rem Bldg 1D86

O FILE EMBASE

3 FILE CAPLUS

L81

L82

TOTAL FOR ALL FILES

3 L78 NOT L52

=> d 1-3 ibib abs

L83 ANSWER 1 OF 3 CAPLUS COPYRIGHT 2005 ACS on STN

2005:158646 CAPLUS ACCESSION NUMBER:

DOCUMENT NUMBER: 142:254587

Methods for treating or preventing autoimmune diseases TITLE:

with 2,4-pyrimidinediamine compounds

Rajinder, Singh; Ankush, Argade; Li, Hui; INVENTOR(S): Bhamidipati, Somasekhar; Carroll, David;

Sylvain, Catherine; Clough, Jeffrey;

Keim, Holger

Rigel Pharmaceuticals, Inc., USA PATENT ASSIGNEE(S):

PCT Int. Appl., 276 pp. SOURCE:

CODEN: PIXXD2

DOCUMENT TYPE: Patent English LANGUAGE:

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION: DAMENTO NO

PAT	ENT	NO.			KINI)]	DATE		i	APPL	ICAT:	ION 1	. 00		D.	ATE	
						-									-		
WO	2005	0168	93		A2		2005	0224	1	NO 2	004-	JS24	716		2	0040	/30
WO	2005	0168	93		A3		2005	0609									
	W:	ΑE,	AG,	ΑL,	AM,	ΑT,	AU,	ΑZ,	BA,	BB,	BG,	BR,	BW,	BY,	ΒZ,	CA,	CH,
		CN,	CO,	CR,	CU,	CZ,	DE,	DK,	DM,	DZ,	EC,	EE,	EG,	ES,	FΙ,	GB,	GD,
		GE,	GH,	GM,	HR,	HU,	ID,	IL,	IN,	IS,	JP,	KE,	KG,	KΡ,	KR,	ΚŻ,	LC,
		LK,	LR,	LS,	LT,	LU,	LV,	MA,	MD,	MG,	MK,	MN,	MW,	MX,	MZ,	NA,	NI,
		NO,	NZ,	OM,	PG,	PH,	PL,	PT,	RO,	RU,	SC,	SD,	SE,	SG,	SK,	SL,	SY,
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		AZ,	BY,	KG,	ΚZ,	MD,	RU,	ТJ,	TM,	AT,	BE,	BG,	CH,	CY,	CZ,	DE,	DK,
		EE,	ES,	FI,	FR,	GB,	GR,	HU,	ΙE,	ΙT,	LU,	MC,	NL,	PL,	PT,	RO,	SE,
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		SN,	TD,	TG													
PRIORITY	APP	LN.	INFO	. :					1	US 2	003-	4916	41P		P 2	0030	730
									1	US 2	003-	5315	98P		P 2	0031	219
									1	US 2	004-	5722	46P		P 2	0040	518

MARPAT 142:254587 OTHER SOURCE(S):

The invention provides methods for treating or preventing autoimmune diseases with 2,4-pyrimidinediamine compds., as well as methods of treating, preventing or ameliorating symptoms associated with such diseases. Specific examples of autoimmune diseases that can be treated or prevented with the compds. include rheumatoid arthritis and/or its associated symptoms, systemic lupus erythematosis and/or its associated symptoms and multiple sclerosis and/or its associated symptoms.

L83 ANSWER 2 OF 3 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2005:120923 CAPLUS

DOCUMENT NUMBER: 142:219300

2,4-Pyrimidinediamines for use in the treatment or TITLE:

prevention of autoimmune diseases

Rajinder, Singh; Ankush, Argade; Li, Hui; INVENTOR(S):

> Bhamidipati, Somasekhar; Carroll, David; Sylvain, Catherine; Clough, Jeffrey;

Keim, Holger

PATENT ASSIGNEE(S): Rigel Pharmaceuticals, Inc., USA

SOURCE:

PCT Int. Appl., 169 pp.

CODEN: PIXXD2

DOCUMENT TYPE:

Patent English

LANGUAGE:

FAMILY ACC. NUM. COUNT: 3

PATENT INFORMATION:

	PATENT NO.						D	DATE		APPLICATION NO. 						DATE			
	WO	WO 2005012294					-	20050210								20040730			
		W:	ΑE,	AG,	AL,	AM,	ΑT,	AU,	ΑZ,	BA,	BB,	BG,	BR,	BW,	BY,	ΒZ,	CA,	CH,	
			CN,	CO,	CR,	CU,	CZ,	DE,	DK,	DM,	DZ,	EC,	EE,	EG,	ES,	FI,	GB,	GD,	
			GE,	GH,	GM,	HR,	ΗU,	ID,	IL,	IN,	IS,	JP,	ΚE,	KG,	KP,	KR,	KZ,	LC,	
			LK,	LR,	LS,	LT,	LU,	LV,	MA,	MD,	MG,	MK,	MN,	MW,	MX,	MZ,	NA,	NI,	
			NO,	NZ,	OM,	PG,	PH,	PL,	PT,	RO,	RU,	SC,	SD,	SE,	SG,	SK,	SL,	SY,	
			ΤJ,	TM,	TN,	TR,	TT,	TZ,	UA,	ŪĠ,	US,	UZ,	VC,	VN,	YU,	ZA,	ZM,	zw	
		RW:	BW,	GH,	GM,	KΕ,	LS,	MW,	MZ,	NA,	SD,	SL,	SZ,	TZ,	UG,	ZM,	ZW,	AM,	
			ΑZ,	BY,	KG,	ΚZ,	MD,	RU,	ТJ,	TM,	ΑT,	BE,	BG,	CH,	CY,	CZ,	DE,	DK,	
			EE,	ES,	FI,	FR,	GB,	GR,	HU,	ΙE,	IT,	LU,	MC,	NL,	PL,	PT,	RO,	SE,	
			SI,	SK,	TR,	BF,	ВJ,	CF,	CG,	CI,	CM,	GΑ,	GN,	GQ,	GW,	ML,	MR,	ΝE,	
			SN,	TD,	TG														
PRIO	RIORITY APPLN. INFO.:								US 2003-491641P					1	P 2	0030	730		
										1	US 2	003-	5315	98P	1	P 2	0031	219	
										1	US 2	004-	5722	46P]	P 2	0040	518	

OTHER SOURCE(S):

MARPAT 142:219300

GΙ

AB The present invention provides methods of treating or preventing autoimmune diseases with 2,4-pyrimidinediamine compds. I [L1, L2 = a direct bond or a linker; R2 = II; R4 = III; X = N, CH; Y, Z = O, S, SO, SO2, etc.; R5 = R6, alkyl, alkenyl, etc.; R6 = H, an electroneg. group, alkoxy, haloalkoxy, etc.; R31 = Me, alkyl; R35 = H, alkyl, cycloalkyl, etc.; or two R35 bonded together to the same carbon atom are taken together to form an oxo, (un)substituted NH], as well as methods of treating, preventing or ameliorating symptoms associated with such diseases. Specific examples of autoimmune diseases that can be treated or prevented with the compds. I include rheumatoid arthritis and/or its associated symptoms, systemic lupus erythematosus and/or its associated symptoms and multiple sclerosis and/or its associated symptoms. The general procedures

III

for synthesis of compds. I are described. The characterization data for over 500 prepared compds. I were given in table. The compds. I were tested in various tests (e.g., inhibition of IgE-induced degranulation, inhibition of Syk kinase, etc.). For example, N4-(2,2-dimethyl-3-oxo-4H-5-pyrido[1,4]oxazin-6-yl)-5-fluoro-N2-(3,4,5-trimethoxyphenyl)-2,4-pyrimidinediamine showed 99.8% inhibition of edema formation when administered at 5 mg/kg in mice.

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L83 ANSWER 3 OF 3 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2004:142963 CAPLUS

DOCUMENT NUMBER: 140:199334

TITLE: Preparation of 2,4-pyrimidinediamines as IgE and/or

IgG receptor modulators for treatment of autoimmune

diseases

INVENTOR(S): Singh, Rajinder; Argade, Ankush; Payan, Donald G.;

Clough, Jeffrey; Keim, Holger; Sylvain,

Catherine; Li, Hui; Bhamidipati,

Somasekhar

PATENT ASSIGNEE(S): Rigel Pharmaceuticals, USA

SOURCE: PCT Int. Appl., 811 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

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OTHER SOURCE(S): MARPAT 140:199334

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AB The present invention provides methods of treating or preventing autoimmune diseases with 2,4-pyrimidinediamine compds., as well as methods of treating, preventing or ameliorating symptoms associated with such diseases. Title compds. I [wherein L1 and L2 = independently a bond or a linker; R2 = (un)substituted alkyl, (hetero)cycloalkyl, or (hetero)aryl; R4 = H or R2; R5 = R6 or (un)substituted alkyl, alkenyl, or alkynyl; R6 = independently H, an electroneg. group, protected alc. or thiol, haloalkyl(oxy), halo, CN, NC, OCN, SCN, NO, NO2, N3, or (un)substituted amino, sulfamoyl(oxy), acyl, carboxy, carbamoyl, (hetero)aryl(alkyl), etc.; with provisos and exclusions; and salts, hydrates, solvates, N-oxides, and prodrugs thereof] were prepared as inhibitors of the IgE and/or IgG receptor signaling cascades that lead to the release of chemical mediators. For example, coupling of 2,4-dichloropyrimidine with 4-ethoxyaniline in EtOH provided N2,N4-bis(4-ethoxyphenyl)-2,4pyrimidinediamine (II). The latter inhibited degranulation of bone marrow derived mast cells challenged with anti-IqE and ionomycin with IC50 values of 4.5 μM and 4.4 μM, resp. Thus, I and their pharmaceutical compns. are useful in the treatment and prevention of diseases characterized by, caused by, or associated with the release of chemical mediators via degranulation of mast, basophil, neutrophil, or eosinophil cells and other processes effected by activation of the IgE and/or IgG receptor signaling cascades. Specific examples of autoimmune diseases that can be treated or prevented with I and their pharmaceutical compns. include rheumatoid arthritis, systemic lupus erythematosis, and multiple sclerosis (no data).

REFERENCE COUNT:

THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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Page 29
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L83
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FULL ESTIMATED COST
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                                                               146.93
DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)
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